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TITLE: Resident Research Associateship Program of the AMRMC

PRINCIPAL INVESTIGATOR: Paul Wilson, Ph.D.

CONTRACTING ORGANIZATION: National Academy of Sciences/NAE/IOM
Washington, DC 20001

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THE NATIONAL ACADEMIES

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Policy and Global Affairs Division
Fellowships Office

December 8, 2009

Ms. Judy Pawlus, Technical Editor
Office of the Deputy Chief of Staff
For Information Management
Attn: MCMR-RMI-S
504 Scott Street
Fort Detrick, MD 21702-5400

Re: Contract No. W81XWH007-2-0001 Technical Report

Dear Ms. Pawlus:

The enclosed technical report is to fulfill our contractual obligations for:

Contract:	**W81XWH007-2-0001**
Title:	**U.S. Army Medical Research and Materiel Command Resident Research Associateship Program**
Contract Period:	**November 1, 2006 – September 30, 2011**

The report covers the period November 1, 2008 through October 31, 2009. This report fulfills contractual requirements for technical reports. The original report and three copies are enclosed for your use.

Sincerely yours,

Judith K. Nyquist, Ph.D.
Deputy Director and
Program Administrator

Enclosures

cc: Mr. Christopher Joyce, USARIEM, Laboratory Program Representative
Michael Dubick, Ph.D., USAISR, Laboratory Program Representative
Robert Kan, Ph.D., USAMRICD, Laboratory Program Representative
Peter Hobart, Ph.D., USAMRIID, Laboratory Program Representative
Sara Rothman, Ph.D., WRAIR, Laboratory Program Representative
Robert Day, Contract Manager, NAS (letter)
Laboratory Contract File (letter)
Laboratory Contract Report File

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National Research Council
RESEARCH ASSOCIATESHIP PROGRAM

with the

U.S. Army Medical Research and Materiel Command (AMRMC)

Annual Contract Technical Report

Report Period: 11/01/08 – 10/31/09

W81XWH007-2-0001

Publicity

The National Academies Research Associateship Programs for the report period were announced to the scientific community in the fall of the preceding year, 2008. Publicity materials describing the National Research Council- U.S. Army Medical Research and Materiel Command [AMRMC]. Programs were distributed in November to presidents, graduate deans, and heads of appropriate science and engineering departments and minority-affairs offices of all academic degree-granting institutions in the United States. An e-mail announcement of the programs was sent to these same contact points prior to each review deadline. Promotional materials were sent to Laboratory Program Representatives, Associateship Advisers, and other interested persons. General advertisements of programs were placed in leading scientific and engineering publications. Publicity materials and other related information were made available on the internet. Research Associateship Programs staff attended numerous professional scientific and engineering meetings and minority recruitment events to promote the various programs and to meet with prospective applicants throughout the year.

Requests

Application materials were distributed in response to specific requests for information about the AMRMC Research Associateship Program or as a result of general requests by persons whose fields of specialization appeared to be appropriate for the research opportunities available in the AMRMC laboratories.

Competition

Panel reviews of applicants for the Research Associateship Programs, including those with the Army Medical Research and Materiel Command are conducted in March, June, September, and/or January of each year. The following is a breakdown of the action taken with the applications during the report period.

	Jan review of Nov app-08	Mar review of Feb app-09	June review of May app-09	Oct review of Aug app-09	TOTAL
TOTAL APPLICATIONS	**6**	**4**	**7**	**10**	**27**
Number of Applications Reviewed	**4**	**2**	**4**	**7**	**17**
Applications not recommended (did not pass Review)	2	2	3	3	**10**
Applications Recommended (passed Review)	**4**	**2**	**4**	**6**	**16**
Awards offered	4	2	4	1	**11**
Awards accepted	4	1	3	1	**9**
Awards declined	0	0	0	0	**0**
Awards withdrawn by RAP (NRC officially withdrew award *after* it had been accepted.)	0	1	1	0	**2**

Associates' Citizenship

Associates on tenure between 11/1/2008 – 10/31/2009 were citizens of the following countries:

35 U.S. Citizens
5 Permanent Residents

1 Japan (Pemanent Resident)
1 Latvia (Perm. Res.)
1 Mauritius (Perm. Resident)
1 England, U.K. (Pending Permanent Resident)
1 China (Pending Perm. Resident)
1 Mauritius (Permanent
1 Resident)
1 Israel (OPT)
2 Brazil (J-1 Research Scholar)
1 India (J-1 Research Scholar)
1 Ireland (J-1 Res. Scholar)
1 Japan (J-1 Research Scholar)
1 Russia (J-1 Research Scholar)

Associates' Activities

Associates who ended tenure during the report period were on tenure for an average of 30 months, ranging from 10 months to 50 months.

Of the 18 Associates who ended tenure during the report period, 14 submitted final reports (78%). In the final reports, Associates indicated the following scholarly activity while on tenure.

- **9** Articles published in refereed journals
- **3** Patent applications
- **11** International presentations
- **28** Domestic presentations
- **2** Awards

After ending their tenure, Associates indicated their future plans as follows:

- **1** Remain at host agency as perm. employee
- **8** Remain at host agency as contract employee
- **0** Research position at other US gov't. lab
- **0** Administrative position at US gov't. lab
- **0** Research position at foreign gov't. lab
- **1** Research/teaching-US college/university
- **1** Research/teaching-foreign college/university
- **1** Research/admin in industry
- **0** Research/admin in non-profit organization
- **0** Postdoctoral research
- **0** Self employed
- **2** Other (may include unemployed)

In their final reports, Associates were asked to evaluate certain aspects of their experiences on a scale of 1 (low) to 10 (high). The average rating for each item follows:

8.64	*Short-term value*	Development of knowledge, skills, and research productivity
8.50	*Long-term value*	How your Research Associateship affected your career to date
8.38	*Laboratory Support*	Equipment, funding, orientation, safety & health training, etc.
7.54	*NRC*	Quality of administrative support from the NRC

Advisers also were asked to complete an evaluation of the Associate. The following summarizes the Adviser evaluations for Associates ending tenure during the report period. Of the 18 Associates who ended tenure, 4 Adviser evaluations were completed 22%. Assessments were made on six criteria using the following rating scale: 1-below average, 2-average, 3-above average, 4-good, and 5-outstanding/exceptional. The average rating for each item follows:

- **3.75** Knowledge of Field
- **4.25** Research Techniques
- **4.25** Motivation
- **4.00** Independent Research
- **4.50** Innovative Thinking
- **4.25** Overall Scientific Ability

The Adviser was asked, "Would you like this Associate as a professional colleague?" The Advisers responded in the following manner:

- **4** Yes
- **0** No
- **0** No Comment
- **0** No Answer

Additional information about the Associates' activities can be found in the attachments described below and the Appendix.

Attachment 1: Associates who were on tenure between 11/07/08 until 10/31/09. Included are the Associate's laboratory center/division location, the starting and termination dates, and the names of their advisers. For those Associates who ended tenure during the report period, it is noted if the final and adviser evaluation reports have been received. Associates are required to submit final reports upon termination of tenure, and advisers are asked to submit a final evaluation of each Associate. Associates who have not submitted a final report have been sent follow-up correspondence.

Attachment 2: All recommended candidates by category (e.g., Recommended, Accepted, No Funding, Declined, etc.). This report includes information about citizenship, the PhD institution, the title of proposed research, proposed or actual starting date, and adviser.

Attachment 3: Summaries of Associate patent activity, if any, and Associate research during tenure as reported on the Associates' termination reports. The summary of patent activity includes the patent application title, inventor(s), and date of application.

Appendix: Final reports received from the Associates who ended tenure during the report period.

US Army Medical Research and Materiel Command

Associate Name+ Adviser	Center	Tenure Dates Start/End	Termination Report	Adviser Report
Alkhalil, Abdulnaser *Dr. M. S. Ibrahim*	(S) U.S. Army Medical Research Institute of Infectious Diseases	6/1/2007 - 5/31/2010		
Altamura, Louis Anthony *Dr. Connie S. Schmaljohn*	U.S. Army Medical Research Institute of Infectious Diseases	3/10/2008 - 3/9/2010		
Andres, Devon Katherine *Dr. Radharaman Ray*	U.S. Army Medical Research Institute of Chemical Defense	5/3/2006 - 9/25/2009	Received	Not Recd
Azeke, John I, Jr. *Dr. Ernest H. Braue, Jr*	U.S. Army Medical Research Institute of Chemical Defense	1/5/2009 - 1/4/2010		
Biggins, Julia Elizabeth *Dr. Gene G. Olinger*	U.S. Army Medical Research Institute of Infectious Diseases	3/19/2007 - 3/18/2010		
Brannan, Jennifer Mary *Dr. Gene G. Olinger*	U.S. Army Medical Research Institute of Infectious Diseases	2/23/2009 - 2/22/2010		
Cashman, Kathleen Anne *Dr. Lisa E. Hensley*	U.S. Army Medical Research Institute of Infectious Diseases	7/11/2005 - 7/31/2009	Not Recd	Not Recd
Dosanjh, Nuvjeevan Singh *Dr. Ashima Saxena*	Walter Reed Army Institute of Research, Silver Spring	4/28/2008 - 2/13/2009	Received	Received
Furtado, Marcio de Araujo *Dr. Debra L. Yourick*	Walter Reed Army Institute of Research, Silver Spring	9/25/2006 - 8/31/2009	Received	Not Recd
Golden, Joseph Walter *Dr. Jay W. Hooper*	U.S. Army Medical Research Institute of Infectious Diseases	4/4/2005 - 5/26/2009	Received	Not Recd
Grant, Rebecca Jean *Dr. Connie S. Schmaljohn*	U.S. Army Medical Research Institute of Infectious Diseases	9/8/2008 - 9/7/2010		
Guarisco, John Arthur *Dr. John H. McDonough*	U.S. Army Medical Research Institute of Chemical Defense	9/6/2007 - 9/5/2010		
Hammerbeck, Christopher David *Dr. Jay W. Hooper*	U.S. Army Medical Research Institute of Infectious Diseases	4/10/2007 - 4/9/2010		
Hathaway, Kyle Christopher *Dr. Julie A. Pavlin*	Walter Reed Army Institute of Research, Silver Spring	6/5/2007 - 6/4/2010		
Herbert, Andrew Scott *Dr. Gene G. Olinger*	U.S. Army Medical Research Institute of Infectious Diseases	4/30/2009 - 4/29/2010		
Honko, Anna Nichole *Dr. Lisa E. Hensley*	U.S. Army Medical Research Institute of Infectious Diseases	6/1/2006 - 11/30/2009		
Jenkins, Amy Lynn *Dr. Susan L. Welkos*	U.S. Army Medical Research Institute of Infectious Diseases	8/13/2007 - 8/12/2010		
Johnston, Sara Christine *Dr. Lisa E. Hensley*	U.S. Army Medical Research Institute of Infectious Diseases	3/25/2009 - 3/24/2010		
Keyser, Brian Michael *Dr. Radharaman Ray*	U.S. Army Medical Research Institute of Chemical Defense	5/4/2006 - 9/25/2009	Received	Not Recd
Koehler, Jeffrey William, Jr *Dr. Connie S. Schmaljohn*	U.S. Army Medical Research Institute of Infectious Diseases	9/17/2007 - 9/16/2010		
Liepinsh, Dmitry *Dr. Urszula Krzych*	Walter Reed Army Institute of Research, Silver Spring	4/18/2006 - 4/17/2009	Received	Not Recd
Ling, Yun *Dr. Ashima Saxena*	Walter Reed Army Institute of Research, Silver Spring	12/4/2006 - 1/3/2009	Received	Received

+ (S) indicates the associate was a Senior.

Associate Name+ Adviser	Center	Tenure Dates Start/End	Termination Report	Adviser Report
McCarthy, Sarah Elizabeth *Dr. John W. Huggins*	U.S. Army Medical Research Institute of Infectious Diseases	4/1/2008 - 3/31/2010		
McCoy, Margaret Ellen *Dr. David E. Lanar*	Walter Reed Army Institute of Research, Silver Spring	7/27/2009 - 7/26/2010		
McGann, Patrick Timothy *Dr. Nikolich P. Mikeljon*	Walter Reed Army Institute of Research, Silver Spring	1/8/2007 - 1/7/2009	Received	Not Recd
Milner, Erin Elizabeth *Dr. Michael P. Kozar*	Walter Reed Army Institute of Research, Silver Spring	7/23/2007 - 7/14/2009	Received	Not Recd
Mitchell, Daniel Anthony *Dr. Connie S. Schmaljohn*	U.S. Army Medical Research Institute of Infectious Diseases	5/14/2008 - 5/13/2010		
Mohan, Govini *Dr. Lucille A. Lumley*	U.S. Army Medical Research Institute of Chemical Defense	7/1/2009 - 6/30/2010		
Muniz, Alberto , Jr. *Dr. Heuy-Ching H. Wang*	Walter Reed Army Institute of Research, Silver Spring	10/14/2008 - 10/13/2010		
Murakami, Yuki *Dr. Frank C. Tortella*	Walter Reed Army Institute of Research, Silver Spring	11/10/2008 - 10/27/2009	Received	Received
Nguyen, Ruth *Dr. Leopoldo C. Cancio*	U.S. Army Institute of Surgical Research	7/6/2009 - 7/5/2010		
Ogg, Monica M. *Dr. Jay W. Hooper*	U.S. Army Medical Research Institute of Infectious Diseases	8/27/2007 - 11/23/2009		
Olivera, Dorian Scott *Dr. Alfred M. Sciuto*	U.S. Army Medical Research Institute of Chemical Defense	11/13/2007 - 2/13/2009	Not Recd	Received
Otto, Tamara Caviston (S) *Dr. David E. Lenz*	U.S. Army Medical Research Institute of Chemical Defense	3/1/2007 - 2/28/2009	Received	Not Recd
Pichugin, Alexander Vladimirovich (S) *Dr. Urszula Krzych*	Walter Reed Army Institute of Research, Silver Spring	1/12/2009 - 1/11/2010		
Reeves, Tony Elvern *Dr. David E. Lenz*	U.S. Army Medical Research Institute of Chemical Defense	6/1/2006 - 5/31/2009	Not Recd	Not Recd
Rose, Rajiv *Dr. Harold G. Klemcke*	U.S. Army Institute of Surgical Research	1/5/2009 - 1/4/2010		
Rossetti, Franco *Dr. Debra L. Yourick*	Walter Reed Army Institute of Research, Silver Spring	6/1/2009 - 5/31/2010		
Schully, Kevin Lee *Dr. Timothy A. Hoover*	U.S. Army Medical Research Institute of Infectious Diseases	5/1/2007 - 4/30/2010		
SillerJackson, Arlene Janel *Dr. Phillip D. Bowman*	U.S. Army Institute of Surgical Research	7/9/2007 - 1/8/2010		
Soojhawon, Iswarduth *Dr. Madhusoodana P. Nambiar*	Walter Reed Army Institute of Research, Silver Spring	6/2/2008 - 6/1/2010		
Spradling, Kimberly Diane *Dr. James F. Dillman, III*	U.S. Army Medical Research Institute of Chemical Defense	7/24/2007 - 7/23/2010		
Taylor, Shannon Lynn *Dr. Connie S. Schmaljohn*	U.S. Army Medical Research Institute of Infectious Diseases	6/8/2005 - 6/7/2009	Received	Not Recd
van de Wetering, Christopher I. *Dr. Patricia L. Worsham*	U.S. Army Medical Research Institute of Infectious Diseases	5/1/2008 - 4/30/2010		

+ (S) indicates the associate was a Senior.

Associate Name+ Adviser	Center	Tenure Dates Start/End	Termination Report	Adviser Report
Wasserberg, Gideon *Dr. Edgar D. Rowton*	Walter Reed Army Institute of Research, Silver Spring	6/13/2008 - 6/5/2009	Received	Not Recd
Yokota, Miyo *Dr. Larry G. Berglund*	(S) U.S. Army Research Institute of Environmental Medicine	3/29/2006 - 9/29/2009	Not Recd	Not Recd
Zeitler, Corinne *Dr. John H. Carra*	U.S. Army Medical Research Institute of Infectious Diseases	1/2/2008 - 1/1/2009	Received	Not Recd

47 Associates Listed

+ (S) indicates the associate was a Senior.

November 2008

A- Accepted Award (4 Applicants listed)

BRANNAN, JENNIFER M
Citizenship: United States
Adviser: Dr. Gene G. Olinger
Research Field: 3298
Research Title: Identification of Host Factors Responsible for Antiviral Response to Ebola Virus Infection

Ph.D. Date: 2008
U of Tex-Health Sci Ctr-Houston
Actual Starting Date: 2/23/09
Termination Date: 2/22/10

HERBERT, ANDREW S
Citizenship: United States
Adviser: Dr. Gene G. Olinger
Research Field: 3298
Research Title: Adjuvant Potential of Immunomodulators Linked to Ebola Antigens Delivered by VEE Replicon Vaccine

Ph.D. Date: 2008
Virginia Polytech Inst & State U
Actual Starting Date: 4/30/09
Termination Date: 4/29/10

JOHNSTON, SARA C
Citizenship: United States
Adviser: Dr. Lisa E. Hensley
Research Field: 3298
Research Title: Identification and Characterization of Viral Immunomodulators That Affect the Host Specificity of Orthopoxviruses

Ph.D. Date: 2009
Univ. of Rochester-Medical Sch/NY
Actual Starting Date: 3/25/09
Termination Date: 3/24/10

ROSSETTI, FRANCO
Citizenship: Brazil
Adviser: Dr. Debra L. Yourick
Research Field: 1829
Research Title: Neurobehavioral and Neuroanatomical Assessment of Organophosphate Exposure

Ph.D. Date: 2008
Sao Paulo, U
Actual Starting Date: 6/01/09
Termination Date: 5/31/10

February 2009

A- Accepted Award

MOHAN, GOVINI
Citizenship: United States
Adviser: Dr. Lucille A. Lumley
Research Field: 1829
Research Title: Evaluation of a Mouse Model of Post Traumatic Stress Disorder and Effects of Novel Neuroprotectants Against Nerve Agent Induced Seizures
Ph.D. Date: 2008
Graduate Center, CUNY
Actual Starting Date: 7/01/09
Termination Date: 6/30/10

W- Withdrew after Review/Recommend

BOWMAN, JOHN J
Citizenship: United States
Adviser: Dr. Sina Bavari
Research Field: 3299
Research Title: Identification of Cellular Kinases Required for Arenavirus Replication
Ph.D. Date: 2008
Harvard University/MA

May 2009

A- Accepted Award (3 Applicants listed)

MCCOY, MARGARET E
Citizenship: United States
Adviser: Dr. David E. Lanar
Research Field: 2740
Research Title: Investigations into the Cross-Presentation of Exogenous Peptides Delivered in Self-Assembling Polypeptide Nanoparticles- Implications for Malaria Vaccine Development
Ph.D. Date: 2009
Va Commonwealth U, Med Coll of Va
Actual Starting Date: 7/27/09
Termination Date: 7/26/10

MELENDREZ, MELANIE C
Citizenship: United States
Adviser: Dr. Julie A. Pavlin
Research Field: 2740
Research Title: Genetic Analysis of Dengue Virus Quasispecies Population Diversity in Thailand: Comparisons in Vector and Host Populations and Potential Correlation with Changing Environmental or Epidemiological Factors
Ph.D. Date: 2009
Montana State University
Expected Starting Date: 1/11/10
Termination Date: 1/10/11

NGUYEN, RUTH
Citizenship: United States
Adviser: Dr. Leopoldo C. Cancio
Research Field: A049
Research Title: Assessment of Sample Entropy as an Endpoint of Resuscitation in a Porcine Model of Hemorrhagic Shock
Ph.D. Date: 2005
University of Kansas
Actual Starting Date: 7/06/09
Termination Date: 7/05/10

May 2009

W- Withdrew after Review/Recommend

NICHOL, KATHRYN E — Ph.D. Date: 2004
Citizenship: United States — Texas A&M University
Adviser: Dr. Nancy J. Wesensten
Research Field: 1827
Research Title: Individual Variations in Vulnerability to Sleep Deprivation and Chronic Sleep Restriction

August 2009

1- Recommended (5 Applicants listed)

DOWER, KEN W — Ph.D. Date: 2004
Citizenship: United States — Brandeis University/MA
Adviser: Dr. Lisa E. Hensley
Research Field: 2740
Research Title: RNAi Screening of Host Factors in Orthopoxvirus Replication and Investigation of miRNA Pathways During Category A Viral Infection

FILONE, CLAIRE MARIE — Ph.D. Date: 2008
Citizenship: United States — University of Pennsylvania
Adviser: Dr. Lisa E. Hensley
Research Field: 3298
Research Title: Identification of Host Factors Necessary for Filovirus Infection

PURKAYASTHA, ANJAN — Ph.D. Date: 2003
Citizenship: India — State Univ of New York at Albany
Adviser: Dr. Lisa E. Hensley
Research Field: 2740
Research Title: Tracking the Population Dynamics of the Monkeypox Virus in Clinical Samples

SIMPSON-HOLLEY, MARTHA R — Ph.D. Date: 2002
Citizenship: England, U.K. — University of Cambridge/England
Adviser: Dr. Lisa E. Hensley
Research Field: 3298
Research Title: Characterization of the Kinetics and Mechanisms of mRNA Decay and Control of Translation during Orthopoxvirus Replication

VIEIRA, REBECCA C — Ph.D. Date: 2008
Citizenship: United States — University of Maryland
Adviser: Dr. Leonard A. Smith
Research Field: 0926
Research Title: Small Molecule Inhibitors of Botulinum Neurotoxin Serotype A

August 2009

A- Accepted Award

LEUNG, LAI YEE
Citizenship: Hong Kong
Adviser: Dr. Frank C. Tortella
Research Field: 1826
Research Title: Characterizing a Clinically/Militarily Relevant Rat Model of Polytrauma Associated with Penetrating Brain Injury: Neuropathological Effects of Transient Hypotension and/or Acute Hypoxemia after Penetrating Ballistic-like Brain Injury

Ph.D. Date: 2009
Wayne State University/MI
Expected Starting Date: 2/08/10
Termination Date: 2/07/11

US Army Medical Research and Materiel Command

Andres, Devon Katherine **5/03/2006 9/25/2009**

1 N-Ac-CRATKML-aldehyde (-CHO; reversible inhibitor) and N-Ac-CRATKML-fluromethylketone (-FMK; irreversible inhibitor) were synthesized as improved forms of BoNT/A peptide inhibitor N-Ac-CRATKML-amide (-NH2).
2 Established two in vitro neuronal cell models for BoNT/A studies: (1) Retinoic acid differentiated human neuroblastoma M17 cells and (2) Dibutyryl c-AMP differentiated neuroblastoma-spinal cord hybid NSC-34 cell line.
3 All three Alexa555-labeled inhibitors permeated through neuronal cell membranes of cultured M17 cells and mouse embryonic spinal cord cells. The -FMK compound was found to be nontoxic in the in vitro M17 cell model and ex vivo/ in vivo models.
4 All three inhibitors significantly reduced the BoNT/A effects on SNAP-25 hydrolysis and inhibition of neurotransmitter release; -FMK was the most promising. Ex vivo/ in vivo studies were performed, but the results were inconclusive.
5 BoNT/A rLC (light chain) activity was inhibited irreversibly by -FMK but not by -NH2; to our knowledge -FMK is the first irreversible BoNT/A inhibitor reported.

Furtado, Marcio de Araujo **9/25/2006 8/31/2009**

1 Formal Training activities at the WRAIR.
2 Study of the following neuroprotectans against organophosphorus induced seizures: N-acetyl-?-aspartylglutamate-4-16 ?M, i.c.v; phenyl-butyl-nitrone-75-150 mg/kg, i.p.; pentoxifylline-60 mg/kg; serine-o-sulfate-50- 100 mg/kg; ifenprodil-10-20 mg/kg.
3 Development of an algorithm to evaluate the large ammounts of telemetry data acquired from rats exposed to organophosphorus compounds
4 Characterization of spontaneous recurrent seizures after seizures induced byorganophosphorus compounds.
5 Publication of relevant findings in peer reviewed journals.

Golden, Joseph Walter **4/04/2005 5/26/2009**

1 Mapped the protective epitope of the L1 molecule
2 Characterized the in vitro mechanism of anti-L1 antibody-mediated orthopoxvirus neutralization
3 Developed an optimized L1R DNA vaccine antigen
4 Developed an in vitro FACS -based assay to detect low levels of anti-L1 antibodies in serum
5 Determined that antibodies elicited by the 4pox DNA vaccine are sufficent for protection and anti-L1 antibodies alone can afford a significant level of protection in the absence of antibodies against the other 4pox targets.

Keyser, Brian Michael **5/04/2006 9/25/2009**

1 Characterized sulfur mustard (SM)-induced apoptosis mechanisms by studying caspase-8, -9, -3 and -6; determined SM EC50 for apoptosis in NHEK cells (skin model), NHBE cells (upper respiratory tract model) and SAEC (deep lung model).
2 Identified the Fas receptor-mediated response as a therapeutic target for SM injury by using selective Fas agonist (CH11) and antagonistic (ZB4) antibodies (Ab). CH11 Ab induces Fas-mediated apoptosis ; ZB4 Ab antagonizes this response.
3 Established a specific Fas intervention approach for vesicant injury by use of small interfering RNA (siRNA) technology.
4 Established siRNA methods to study cross talk between caspases (-8, -9, -3, -6) in a collaborative project on on caspase signaling amplification loop as a newly identified SM mechanism of action in airway injury.
5 Demonstrated a post SM exposure siRNA therapeutic window in a cell culture model and provided further support for the SM-induced Fas response amplification loop.

Liepinsh, Dmitry **4/18/2006 4/17/2009**

1 Performed study on P.bergei malaria antigen presentation using transporter associated with antigen processing (TAP) knockout (KO) mouse model.
2 Contributed to work studying differences in T cell responses between gamma-irradiated sporozoite (g-spz) and UIS3/4 KO spz immune mice.

US Army Medical Research and Materiel Command

Liepinsh, Dmitry **4/18/2006 4/17/2009**

3 Generated a tool to study liver stage antigen presentation in a rodent model of malaria (CD8 T-cell hybridomas specific for liver stage peptides and/or responding to liver dendritic cells obtained from g-spz immune/challenged animals).
4 Obtained preliminary data on P.berghei spz entry into activated macrophages and hepatocytes in vitro.
5 Contributed to the work investigating the importance of IL-15 for the maintenance of memory T cells and the role of lymphoid liver DCs in the induction of protective immunity in P.berghei model of malaria.

Ling, Yun **12/04/2006 1/03/2009**

1 I used molecular dynamics modeling to construct more than fifty 3-D atomic structures of oxime-nerve-agent-inhibited human AChE complexes.
2 Using the models I built, I quantitatively and structurally explained the different reactivating abilities of 2-PAM and MMB4.
3 I constructed fourteen different human AChE mutants and expressed one of them in mammallian cells. Another two expressions were not successful due to undetermined reasons.
4 I configured, calibrated, and optimized the Tecan automation robot for the "Screening of novel reactivator project" and other projects.
5 I instructed and helped my colleagues to use the Tecan Freedom Evo machine.

McGann, Patrick Timothy **1/08/2007 1/07/2009**

1 Development of a new media for the rapid growth of Francisella species.
2 Full transciptome analysis of F. tularensis following exposure to Acid Oxidation and Temperature insults.
3 Transcriptome comparison of virulent Type A and less virulent Type B strain in response to environemental stress.
4 Development of a novel full genome qRT-PCR array with the J. Craig Ventner Institute.
5 Full transcriptome analysis of highly virulent Type A and virulent Type B strains following macrophage infection.

Milner, Erin Elizabeth **7/23/2007 7/14/2009**

1 Synthesized over 350 quinoline methanol analogs, many of which have promising in vivo efficacy
2 Co-authored a lead optimization proposal and submitted to Medicines for Malaria Venture (MMV)
3 MMV Proposal was accepted, CRADA will be signed late June 2009, and $1M in funds will be awarded
4 Collaborated with U Monash to determine blood-brain barrier permeability of specific chemotypes of the scaffold
5 Collaborated with U Dundee to determine the bound/unbound variations of specific chemotypes of the scaffold

Murakami, Yuki **11/10/2008 10/27/2009**

1 Set up the brain tissue oxygen tension measurement in normal rats.
2 Determined the brain tissue oxygen tension following the penetrating ballistic-like brain injury.
3 Determined the effect of selective brain cooling on brain tissue oxygen tension in normal rat.
4 Determined the effect of selective brain cooling on brain tissue oxygen tension following penetrating ballistic-like injury.

Otto, Tamara Caviston **3/01/2007 2/28/2009**

1 1) Generated and expressed mutants of human paraoxonase 1 (HuPON1) in 293T cells.
2 2) Determined that VR acts as a competitive inhibitor of paraoxon and a non-competitive inhibitor of VX with the H115W
variant of HuPON1.
3 3) Analyzed wild type HuPON1 and five variants of HuPON1 with five V-agent analogs to gain an understanding of the active
site of the enzyme.
4 4) Determined that as the molecular volume of the retained group of the V-agent analogs increased, the binding affinity of
wild type HuPON1 enzyme improved by as much as four-fold.

Otto, Tamara Caviston **3/01/2007 2/28/2009**

5 5) Demonstrated that as the molecular volume of the leaving group of the V-agent analogs decreased, the catalytic capacity of
the wild type HuPON1 progressively decreased by about five-fold.

Taylor, Shannon Lynn **6/08/2005 6/07/2009**

1 The hantavirus Andes, is able to inhibit phosphorylation of STAT1 and STAT2 and activation of the interferon (IFN) pathway during infection.
2 Our results indicate that Crimean congo hemorrhagic fever virus activates the transcription factor IRF-3 thus allowing for transcription and production of IFN. This IFN made during infection retains its ability to phosphorylate STATs.
3 The hanvtavirus Hantaan, is also able toinhibit phosphorylation of STAT1 and STAT2 and activation of the IFN pathway during infection. Furthermore, it can also prevent tumor necrosis factor alpha (TNF-a) induced activation of NF-kB.
4 Importin alpha is a transport protein required for binding to NF-kB and transporting it from the cytoplasm to the nucleus so it can initiate transcription of inflammatory genes required for an antiviral effect.
5 The protein responsible for this inhibition is the Hantaan virus nucleocapsid. Nucleocapsid binds to the protein importin alpha and prevents it from transporting NF-kB into the nucleus and thus antagonizing the pathway.

Wasserberg, Gideon **6/13/2008 6/05/2009**

1 Attractant assay: Screened a wide variety of monofloral honeis and identified a few strong attractant on which further work will be done.
2 Systemic and Feed-through control: we studied the feed-through effectiveness of the insecticide Imidaclorpid on larval sand flies feeding on feces of rodent treated with the insecticide. Results, showed strong insectidial activity of the chemical.
3 Sand fly ovisposition attractants. 2-way factorial design experiment on the effect of eggs and frass on oviposition rate of Lutzomyia longipalpis and Phelebotomus papatasi. Current status: frass extracts have stronge effect.
4 Evaluation of sand fly trapping methods. We compare in the field constant flow to pulsed flow of CO2 on sand fly trapping rate using standard CDC traps. Status: Pilot conducted during summer of 2008, further trapping under way.

Zeitler, Corinne **1/02/2008 1/01/2009**

1 Cloned viral domain into several expression vectors.
2 Cloned polymerase domain into several expression vectors.
3 Cloned viral domain + polymerase into several expression vectors.
4 Purified viral domain from insoluble portion.
5 Purification of soluble polymerase.

3) Neuroblastoma-spinal cord hybrid NSC-34 cell line as a neuronal model to study botulinum neurotoxins. Andres D., Keyser B., Benton B., and Ray R. (In preparation).

4) Fas Antagonism Markedly Attenuates Sulfur Mustard-Induced Apoptosis in Normal Human Airway Epithelial Cells Keyser B. , Andres D., Benton B., Carpin C., and Ray R. (In preparation).

10) *PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH*
Provide titles, inventors, and dates of applications.

11) *PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES*
Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.

International

Oral Presentation:
A Novel Irreversible Peptide Inhibitor to Counteract Botulinum Neurotoxin A (BoNT/A) Poisoning In Vitro. Botulinum Research Center, 3rd Annual Symposium, Univeristy of Massachuesetts, Dartmouth, MA, August 2009.

Domestic

Posters:
D. Andres, B. Keyser, P. Zhang, B. Benton, S. Hauck, P. Ray, R. Ray.
A Novel Irreversible Peptide Inhibitor to Counteract Botulinum Neurotoxin A (BoNT/A) Poisoning In Vitro.
FASEB Journal, 23:676.8, 2009. Experimental Biology, New Orleans, LA

D. Andres, B. Keyser, P. Zhang, B. Benton, St. Hauck, P. Ray, R. Ray. Evaluation of Short Peptide Inhibitors to Counteract Botulinum Neurotoxin A (BoNT/A) Poisoning in Vitro. FASEB Journel; 22:792.11, 2008. Experimental Biology, San Diego, CA. and BioScience Biennial Meeting, Hunt Valley MD, June 2008.

B. Keyser, D. Andres, B. Benton, R. Ray. Fas targeted siRNA markedly attenuates sulfur mustard-induced apoptosis in human airwary epithelial cells. FASEB Journal, 22:648.18, 2008. Experimental Biology, San Diego, CA and BioScience Biennial Meeting, Hunt Valley MD, June 2008.

R. Ray, B. Keyser, D. Andres, S. Hauck, B. Benton, C. Carpin, A. Daher, C. Simbulan-Rosenthal, D. Rosenthal. Human bronchial/tracheal epithelial cells (BEC) are more sensitive than small airway epithelial cells (SAEC) to sulfur mustard-induced apoptosis apparently due to a Fas(death receptor) response amplification loop. Experimental Biology 2008 abstract, and BioScience Review 2008 abstract, Hunt Valley MD, June 2008.

B. Keyser, D. Andres, C. Carpin, B. Benton, R. Ray. Fas agonist antibody CH11 enhances apoptosis in sulfur mustard-exposed human keratinocytes and airway epithelial cells. Experimental Biology Annual Meeting, Washington DC, 2007

12) *SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES* **Include dates, names and locations of seminars.**

13) *PROFESSIONAL AWARDS RECEIVED DURING TENURE*

14) *POST-TENURE POSITION / JOB TITLE*

Research Scientist, ORISE contractor

15) *NAME AND ADDRESS OF POST-TENURE POSITION / JOB ORGANIZATION*

USAMRICD
3100 Ricketts Point Rd
APG, MD 21010

16) *POST-TENURE POSITION STATUS / CATEGORY* **Please indicate only one.**

☐ Remain at Host Agency as Permanent Employee
☒ Remain at Host Agency as Contract/Temporary Employee
Abbreviate Host Laboratory/Center **USAMRICD**
☐ Research Position at Another US Government Laboratory
☐ Administrative Position at US Government Laboratory
☐ Research Position at Foreign Government Laboratory

☐ Research/Teaching at US College/University
☐ Research/Teaching at Foreign College/University
☐ Research/Administration in Industry
☐ Research/Administration in Non-Profit Organization
☐ Postdoctoral Research
☐ Self Employed
☐ Other: specify _____

17) *APPRAISAL OF RESEARCH ASSOCIATESHIP PROGRAM*

On a scale of 1 – 10 (poor - excellent), please rate the following:

SHORT TERM VALUE

10 Development of knowledge, skills, and research productivity

Comments

Became knowledgable in neuroscience, toxicology, and chemical/biological threats and interventions.

LONG TERM VALUE

10 How the NRC Associateship award affected your career to date

Comments

Received effective training to function as an independent investigator.

LAB SUPPORT

10 Quality of support from the Laboratory--equipment, funding, orientation, safety and health guidelines, etc.

Comments

Excellent support in terms of research opportunity, collaboration, and administrative assistance.

ADVISER/MENTOR SUPPORT

10 Quality of mentoring from the Laboratory NRC Adviser (USMA Mentor, if applicable)

Comments

Dr. Radharaman Ray was an excellent mentor. I have grown professionaly under his tutelage.

LPR SUPPORT

9 Quality of administrative support from the Laboratory (e.g., NIST) NRC Program Representative (LPR)

Comments

Suggest improved communication.

NRC SUPPORT

7 Quality of administrative support (applications, inquiries, post-review, award-related, travel, etc.) from the NRC

Comments

Improve coordination in accounting and communication between NRC office and the fellows

18) *PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT.*

See above comments.

Mail & Delivery Address

It is NOT necessary to mail the original.

The National Academies
NRC Research Associateship Programs
500 Fifth Street NW, #568
Washington, DC 20001

This form SHOULD be E-MAILED directly to the NRC Coordinator.

http://www7.national-academies.org/rap/Coordinators_with_Agencies.html
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Rev. Jan. 2008

Suggestions for, or problems with, forms should be directed to the forms manager, Suzanne White, swhite@nas.edu.

ID#

CC#

b) **Books, book chapters, other publications**

—

c) **Manuscripts in preparation, manuscripts submitted**

—

10 *PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM THE NRC ASSOCIATESHIP RESEARCH PROGRAM*
Provide titles, inventors, and dates of applications.

—

11) *PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES*
Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.

International

—

Domestic

—

12) *SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES* **Include dates, names and locations of seminars.**

—

13) *PROFESSIONAL AWARDS RECEIVED DURING TENURE*

—

14) *POST-TENURE POSITION TITLE*

Scientist, Pharmaceutical Sciences

15) *POST-TENURE ORGANIZATION* **Provide name and city of organization.**

Protein-Potential, Rockville, Maryland.

16) *POST-TENURE POSITION STATUS / CATEGORY* **Please indicate only one.**

- ☐ Remain at Host Agency as Permanent Employee
- ☐ Remain at Host Agency as Contract/Temporary Employee

Abbreviate Host Laboratory/Center____

- ☐ Research Position at Another US Government Laboratory
- ☐ Administrative Position at US Government Laboratory
- ☐ Research Position at Foreign Government Laboratory
- ☐ Research/Teaching at US College/University
- ☐ Research/Teaching at Foreign College/University
- ☑ Research/Administration in Industry
- ☐ Research/Admin in Non-Profit Organization
- ☐ Postdoctoral Research
- ☐ Self Employed
- ☐ Other: specify _____

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17) *APPRAISAL OF NRC RESEARCH ASSOCIATESHIP PROGRAM*
On a scale of 1 – 10 (poor - excellent), please rate the following:

SHORT TERM VALUE

0 Development of knowledge, skills, and research productivity
Comments

6

LONG TERM VALUE

0 How the National Academies Associateship award affected your career to date
Comments

6

LAB SUPPORT

0 Quality of support--equipment, funding, orientation, safety and health guidelines, etc.
Comments

9

ADVISER / MENTOR SUPPORT

0 Quality of mentoring from the Lab NRC Adviser (USMA Mentor, if applicable)
Comments

9

LPR SUPPORT

0 Quality administrative support from the LPR
Comments

9

NRC SUPPORT

0 Quality of administrative support from the NRC
Comments

9

18) *PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT.*

Recurrent Seizures even with Initial Oxime, Atropine and Diazepam Therapeutics. HFM-149/RTO Symposium, 2007. Defense Against the Effects of Chemical Hazards: Toxicology, Diagnosis and Medical Countermeasures.

Furtado, MD; Lumley, L; Waterhouse, J; Lichtenstein, S; Litwack, B; Herbert, T; Clements, K; Robison, C; Yourick, D. Spectral Evaluation of Electrographic Seizures after Exposure to Organophosphorus Compounds. 2279, The Toxicologist CD — An official Journal of the Society of Toxicology, Volume 102, Number S-1, March 2008. http://www.toxicology.org/ai/pub/Tox/2008Tox.pdf

c) Manuscripts in preparation, manuscripts submitted

Furtado MD, Lumley L, Robison C, Tong LC, Yourick D. Spontaneous recurrent seizures after status epilepticus induced by soman in Sprague-Dawley rats. Article re-submitted to Epilepsia.

Behavioral and Neuropathologic Outcomes after Ifenprodil Treatment in Soman-exposed Rats. To be submitted to the European Journal of Pharmacology.

10) *PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NATIONAL ACADEMIES ASSOCIATESHIP RESEARCH*
Provide titles, inventors, and dates of applications.

N/A

11) *PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES*
Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.

International

Abstract, HFM-149/RTO Symposium, Defense Against the Effects of Chemical Hazards: Toxicology, Diagnosis and Medical Countermeasures

STUDIES TO EVALUATE NOVEL NEUROPROTECTANTS IN A RAT MODEL OF SOMAN EXPOSURE REVEAL EPISODES OF STATUS EPILEPTICUS AND SPONTANEOUS RECURRENT SEIZURES EVEN WITH INITIAL OXIME, ATROPINE AND DIAZEPAM THERAPEUTICS

1Yourick, D.L., 1Furtado M., 1Nagode D., 1Cohn S., 1Bauman R.A., 2Robison C.L., 1,2Tong L., and 2Lumley L.A. 1Walter Reed Army Institute of Research, 503 Robert Grant Ave., Silver Spring, MD and the 2U.S. Army Medical Research Institute of Chemical Defense, Aberdeen Proving Ground, MD, U.S.A.

Introduction and Rationale: The threat of exposure to organophosphorus (OP) nerve agents exists on the battlefield, as a result of terrorism, and as part of current demilitarization efforts. Control of seizures resulting from OP exposure and means to mitigate central nervous system damage continue to be a major military and civilian research goal. Status epilepticus (SE), a primary outcome of exposure to OP nerve agents, triggers a pathophysiological cascade of central nervous system molecular events beginning with elevated cholinergic drive followed by excitotoxicity, oxidative damage and neuronal loss.
Method: The classes of potential neuroprotective compounds currently being evaluated include NR2B-selective antagonists, serine racemase inhibitors, nitrone-based free radical spin-trappers, glutamate carboxypeptidase II inhibitors/glutamate effectors, and GABAergic enhancers. Our well defined rodent in vivo model of soman exposure includes HI-6 pretreatment and atropine (1 min) and diazepam/neuroprotectant (30 minute) post-exposure treatments. The extended post-exposure monitoring period being used has allowed observation of the occurrence of seizures and EEG anomalies for 14 days after soman, a critical and novel approach for determining long-term treatment outcomes. Using an array of powerful telemetric acquisition and analysis software, detection, characterization, and quantification of epileptiform activity is enhanced and optimized for time and frequency resolution during this post-exposure period. Behavioral studies for selected studies include beam walk and Morris water maze.
Results: As much as 40% of rats experienced spontaneous recurrent seizures (throughout the post-exposure testing period) and additional episodes of SE, usually within 3 days of soman exposure. Histopathological data revealed severe tissue damage in cortical and sub-cortical areas that was directly correlated with secondary SE events occurring several days after exposure. In terms of behavioral outcomes, the NR2B-selective antagonist ifenprodil and the serine racemase inhibitor serine O-sulfate (SOS) provided improved functional recovery, in preliminary analyses, on the beam walk test. SOS reduced mortality. Additional data as to neuroprotective efficacy of selected compounds will be presented.
Conclusion: Reduced neuropathology, morbidity and mortality may be achievable through appropriate neuroprotective therapeutics. Extended EEG monitoring may be needed in studies identifying novel therapeutics and in clinical evaluation of nerve-agent exposed casualties. Non-convulsive and convulsive seizures may exacerbate damage and continuing therapeutic interventions with anticonvulsants and neuroprotectants, due to late and continuing seizure events, may be required.

Support Contributed By: Defense Threat Reduction Agency

Abstract, I CONGRESS IBRO/LARC OF NEUROSCIENCES FOR LATIN AMERICA, CARIBBEAN AND IBERIAN PENINSULA (I CONGRESS IBRO/LARC OF NEUROSCIENCES FOR LATIN AMERICA, CARIBBEAN AND IBERIAN PENINSULA (September 2008 ; Buzios, RJ, Brazil)

Evaluation of activity and body temperature after seizures induced by organophosphorous compounds in sprague-dawley rats.

Furtado, Marcio1; Lumley, Lucille2; Sedigh-Sarvestani, Madineh1; Zheng, Andy1; Clements, Kristin1; Robison, Christopher2; Yourick, Debra1 - 1Walter Reed Army Institute of Research - Headquarters / Res. Mark. Dev.; 2U.S. Army Medical Research Institute of Chemical Defense.

The understanding of the mechanisms of propagation of status epilepticus (SE) induced by organophosphorus (OP) compounds and the search for neuroprotectants are essential for the advance of the knowledge in this field and to avoid casualties in an eventual incident. The exposure to toxic levels of OP nerve agents inhibits cholinesterase and induces SE and death. Control of seizures induced by OP and means to mitigate central nervous system damage continue to be major military and civilian research goals. Exposure to soman causes brain damage as a result of SE. Our laboratory has been assessing the neuroprotective effects of novel therapeutics post soman exposure in rodents by characterizing electrophysiological and behavioral seizures, motor performance, and neuropathology. In the present study, we characterized long-term EEG, activity and temperature changes after SE induced by OP. Male rats were implanted with telemetry transmitters and after 7 days of recovery were pretreated with the oxime HI-6 (125 mg/kg, i.p.) 30 min before the injection of soman (110 µg/kg, s.c.). One min after soman administration, rats were injected with atropine SO4 (2 mg/kg, i.m.). At 30 min post soman exposure, diazepam (DZP, 10 mg/kg, s.c.) was injected for treatment of SE. Following the injection of DZP, a group of animals received a potential neuroprotectant or its vehicle. EEG, activity and temperature were recorded continuously for at least 2 days of baseline and fifteen days after soman exposure. The average latency for soman-induced seizures was (8.29 ± 1.82 min; STD; n=235 rats). The core body temperature decreased after the exposure, but returned to basal levels 24 hours after exposure. A disruption of the circadian cycle both on temperature and activity was noticed during up to 3 days after SE. Also, the increase on activity observed during this period was usually followed by electrographic seizures. At the same time, a marked increase on the power spectra on the EEG delta band (0.1 – 4 Hz) was also noticed. In a long term window the activity increased both during the day and night time among the rats that developed SE (79.6 %). These persistent changes in the activity pattern are suggestive of long term modifications in the exploratory behavior. Finally, rats that developed SE had marked brain damage. Continuous seizure activity persisted even after the injection of DZP + potential neuroprotectant and appears to be the main cause of brain damage. Rats that did not develop SE (20.4 %) did not show long term alterations in the activity.

Domestic

Abstract, Annual meeting of Society for Neuroscience, San Diego, CA, 2007.

Evaluation of and therapeutic approaches to behavioral and electrographic seizures after exposure to organophosphorus compounds

M.D. FURTADO1, L.A. LUMLEY2, R. A. BAUMAN1, S. COHN1, D. NAGODE1, J. WATERHOUSE1, L. TONG2, C. ROBISON2, D.L. YOURICK1
1Walter Reed Army Institute of Research, Silver Spring, MD, 2Pharmacology, U.S. Army Medical Research Institute of Chemical Defense, Aberdeen Proving Ground, MD.

The threat of exposure to organophosphorus (OP) nerve agents exists on the battlefield, as a result of terrorism, and as part of current demilitarization efforts. Control of seizures resulting from OP exposure and means to mitigate central nervous system damage continue to be major military and civilian research goals. Soman exposure induces status epilepticus (SE), through magnification of cholinergic drive followed by excitatory amino-acid-induced brain injury. N-Acetyl-β-aspartylglutamate (β-NAAG) is a potential neuroprotectant since efficacy has been shown against hypoxia- and NMDA-induced injury in vitro and ischemic spinal cord injury in vivo. The likely mechanism for this protection is low potency NMDA-agonist activity turned antagonist activity when Glu concentrations are high. Antioxidants such as phenyl t-butyl nitrone (PBN) have also been suggested as therapeutic intervention for oxidant damage as a consequence of soman-induced injury. Male rats were pretreated with the oxime HI-6 (125 mg/kg, i.p.) 30 min before the injection of soman (110 µg/kg, s.c.). One min after soman exposure, rats were injected with atropine SO4 (2 mg/kg, i.m.). At 30 min post soman exposure, diazepam (DZP, 10 mg/kg, s.c.) was injected for treatment of SE. Following the injection of DZP, a group of animals (n=13) received β-NAAG (4 and 8 µmols, i.c.v.) or its vehicle. PBN (75 mg/kg) was tested in the same model of soman exposure and available therapeutics. Fifteen days after exposure all animals were euthanized and their brains removed. Through the use of a customized Matlab program (Mathworks, Vers. 7) time spent in electrographic seizures was estimated. We found a strong correlation between time spent in seizures during the 1st day and brain damage quantified by silver staining. Unexpectedly, PBN-treated rats spent more time in seizures than controls, suggesting a pro-convulsive effect of this compound. β-NAAG-treated rats (8 µmols) spent less time in seizure than controls during the 1st day. Spontaneous recurrent seizures (SRS) were detected in both control and β-NAAG-treated rats with no statistical difference between groups. There was a strong correlation between time spent in seizure 24 hr after exposure and the number of SRS. While analysis continues, these data suggest that β-NAAG may be efficacious as a neuroprotectant against soman-induced seizures. Also, the continuous seizure activity that persists even after the injection of DZP appears to be the main cause of brain damage and SRS. Neuropathological assessments are ongoing in β-NAAG and PBN groups.

Pretreatment with 17β-estradiol reduces seizures and brain pathology in rats exposed to the chemical warfare nerve agents VX and soman.

Lumley LA1, Robison CL1, Furtado M1, Tong L1, Shih T-M1, Dill T1, Somsamayvong B1, Saviolakis GA2, Yourick DL2.
1Research Division, US Army Medical Research Institute of Chemical Defense, Aberdeen Proving Ground, MD, USA;
2Walter Reed Army Institute of Research, Silver Spring, MD, USA

Chemical warfare nerve agents are toxic organophosphorus compounds that irreversibly inhibit acetylcholinesterase, leading to accumulation of acetylcholine at peripheral and central synapses. One of the most harmful responses to toxic levels of nerve agents is prolonged seizures that can lead to extensive brain pathology. Although current treatments for nerve agent toxicity promote survival, they also have unwanted side effects, have a narrow window of opportunity and are not fully neuroprotective. There is need for identifying adjunct therapeutics to reduce or prevent brain damage and performance deficits subsequent to nerve-agent induced seizures. We implemented a rat model of VX and soman toxicity to screen compounds for functional neuroprotection against nerve agents. The steroid hormone 17β-estradiol has been reported to have potent neuroprotective activity in a variety of in vivo and in vitro models, including ischemia and excitotoxicity. We evaluated 17β-estradiol for its protective efficacy against toxic doses of soman and VX using endpoints of EEG, neuropathology and behavioral assessments. Male rats pretreated with 17β-estradiol (0.1 mg/kg, sc) were exposed to 1.6 LD50 VX 30 min later, followed by atropine sulfate, the oxime 2-PAM and the anticonvulsant diazepam. Rats pretreated with 17β-estradiol had reduced seizure activity and brain pathology compared with rats that did not receive 17β-estradiol. Similar findings were observed in rats pretreated with 17β-estradiol prior to exposure to 1.0 LD50 soman. These findings show that 17β-estradiol pretreatment in addition to atropine, an oxime and diazepam treatment reduced seizures and brain pathology in soman-exposed rats to a greater extent than treatment with an atropine, an oxime and diazepam.

Support Contributed By: DTRA to Lucille A. Lumley

Society of Toxicology Meeting, 2008, Seattle, WA

TITLE: SPECTRAL EVALUATION OF ELECTROGRAPHIC SEIZURES AFTER EXPOSURE TO ORGANOPHOSPHORUS COMPOUNDS

AUTHORS (LAST NAME, FIRST NAME): Furtado, Marcio1; Lumley, Lucille2; Waterhouse, Jamie1; Lichtenstein, Spencer1; Litwack, Benjamin1; Herbert, Terena1; Clements, Kristin1; Robison, Christopher2; Yourick, Debra1
SPONSOR NAME: Jeffrey Yourick
INSTITUTIONS (ALL): 1. Headquarters, Walter Reed Army Institute of Research, Silver Spring, MD, USA.
2. U.S. Army Medical Research Institute of Chemical Defense, Aberdeen Proving Ground, MD, USA.

ABSTRACT BODY: The potential for exposure to organophosphorus (OP) nerve agents exists on the battlefield and even in urban areas due to the current terrorist's threats. Control of seizures induced by OP and means to mitigate central nervous system damage continue to be major military and civilian research goals. Soman exposure induces status epilepticus (SE), through overexcitation of cholinergic pathways followed by excitatory amino-acid-induced brain injury. N-Acetyl-β-aspartylglutamate (β-NAAG) already showed efficacy against hypoxia- and NMDA-induced injury in vitro and ischemic spinal cord injury in vivo. Male rats were pretreated with the oxime HI-6 (125 mg/kg, i.p.) 30 min before the injection of soman (110 µg/kg, s.c.). One min after soman exposure, rats were injected with atropine SO4 (2 mg/kg, i.m.). At 30 min post soman exposure, diazepam (DZP, 10 mg/kg, s.c.) was injected for treatment of SE. Following the injection of DZP, a group of animals received β-NAAG (4 and 8 µmols, i.c.v.) or its vehicle. EEG was recorded 24 hours/day for fifteen days. At this time, all exposed animals were euthanized and their brains removed and processed for silver staining. Through the use of a customized Matlab program (Mathworks, Vers. 7), alterations in the EEG power spectra were evaluated. Magnitude of the power spectra on delta band remained increased in rats that had SE. This alteration persisted during all the entire observation period. β-NAAG-treated rats (8 µmols) had a reduction in the power spectra on delta band and also in electrographic seizure activity during the 1st day after exposure. However, these rats still showed marked brain damage. Continuous seizure activity persisted even after the injection of DZP + neuroprotectant and appears to be the main cause of brain damage. Therefore, repeated treatment with anticonvulsants/neuroprotectants may be needed to reduce or avoid OP neuroexcitotoxicity.

Bioscience Review 2008, Hunt Valley, MD

Longer-Term EEG Recording and Analysis by an Unsupervised Algorithm for Continuous Monitoring

Marcio Furtado1, Madineh Sarvestani1, Lucille A. Lumley2, Andy Zheng2, and Debra Yourick1. 1Headquarters, Walter Reed Army Institute of Research, Silver Spring, MD, USA.

2U.S. Army Medical Research Institute of Chemical Defense, Aberdeen Proving Ground, MD, USA.

The organophosphorous compound soman is an acetylcholinesterase inhibitor that is highly damaging to cells in the central nervous system. Exposure to soman causes damage as a result of convulsions and seizures. Our laboratory has been assessing the neuroprotective effects of novel therapeutics post soman exposure in rodents by characterizing electrophysiological and behavioral seizures, motor performance, and neuropathology. In the present study, changes in long-term recordings of cortical EEG were used as a model to evaluate the potential of neuroprotective drugs as antagonists for soman-induced seizures. Rats were implanted with wireless monitoring transmitters and exposed to soman followed by treatment with therapeutics similar to those administered in the field after nerve agent exposure. The resulting EEGs were recorded continuously for fifteen days. Long-term EEG recordings are rarely performed, and often unavailable, due to the large volume of data gathered and the subsequent need to analyze this data in an accurate and time-efficient manner. Furthermore, the large amount of data and the presence of artifacts preclude the use of many third-party EEG analysis software tools.
An unsupervised Matlab algorithm has been developed that removes artifacts and measures the spatial (time analysis), spectral (frequency analysis), and combined (wavelet analysis) characteristics of long-term EEG recordings. The algorithm uses the method of short-time Fourier transform to compute the power spectrum of the signal for two second intervals. The spectrum is then divided into the delta, theta, alpha, and beta frequency bands and the maximum energy value in each band is recorded. The maximum energy value of thirty two-second intervals is then averaged to give an overall energy value for a one-minute interval. In this way, both the spatial and spectral characteristics of the original signal are preserved and a graph of average energy of the signal over the entire duration of the recording is obtained.
Artifact removal is based on a linear fit to the power spectrum of the short two-second time windows. Artifacts generally contain much higher amplitudes and frequencies than normal EEG data. As a result, the power spectrum of an artifact is easily differentiated from that of authentic EEG activity.
In order to visually verify our method of artifact removal, a graphical user interface has been created that simultaneously plots the raw EEG in time, the power spectrum of the EEG, and the plot of the wavelet transform of the EEG. The accuracy of this algorithm for artifact removal and seizure detection is also verified against visual inspection of video recordings of rodents. These videos are a good predictor of electrographic activity since they indicate the behavioral manifestation of seizures (see related presentation by Clements et. al).

Changes in time spent in seizure are a powerful indicator of the neuroprotective effects of novel therapeutics against organophosphate exposure. However, since exposure to soman causes acute and chronic damage, any suitable evaluation

model must assess the neuroprotective effect of the therapeutic agent with acute and chronic continuous EEG monitoring. Thus, monitoring EEG for a time period of one or two days post exposure, as is prevalent in the field of nerve agent studies, is likely not a comprehensive indicator of the neuroprotective effects of therapeutic agents. Using our unsupervised algorithm, it is possible to record and analyze continuous long-term EEG recordings in a time-efficient and accurate manner. The full analysis will be illustrated and discussed.

This work was supported by the U.S. Army Medical Research and Materiel Command and the Defense Threat Reduction Agency under Grant # 1.E0042_08_WR_C and previously funded grants from these sources.

Behavioral, Physiological and Neuropathological Effects of Exposure to Sarin: Dependence on Seizures

Theresa M. Ward1, Christopher L. Robison1, Stephen P. Estes1, Kristen L. Kamberger1, Marcio D. Furtado2, Santresda M. Johnson1, Madineh Sedigh-Sarvestani2, Debra L. Yourick2, Tsung-Ming Shih1, Lucille A. Lumley1 US Army Medical Research Institute of Chemical Defense, Aberdeen Proving Ground, MD, USA; 2Walter Reed Army Institute of Research, Silver Spring, MD, USA

We developed a rat model of sarin (GB) toxicity for use in screening neuroprotective drugs and for genomics studies. The goal was to develop a model of exposure to toxic levels of GB that did not include any pretreatments, yet in which a large number of rats survive the exposure. We administered 1.0 LD50 GB to rats and then treated the rats with atropine sulfate (ATR; 2 mg/kg, im) and 2-PAM (25 mg/kg, im) either 1 or 15 min and diazepam (DZP; 10 mg/kg, sc) 30 min after the appearance of toxic signs. We used telemetry to record EEG, temperature and activity continuously (24 hr/day). In rats that displayed seizures, the average latency to seize was 7.2 minutes. In rats that received ATR and 2-PAM 1 min after the appearance of toxic signs, 50% of the rats displayed seizures and survived, while 25% did not display seizures, and 25% displayed seizures and did not survive. In those with delayed (15 min) treatment 86% seized, but with only 29% of those seizing survived.

The majority of damage following nerve agent exposure is considered to be a result of prolonged seizure activity. Exposure to 1.0 LD50 GB (with ATR, 2-PAM and DZP treatment) resulted in severe neuronal tract degeneration in the piriform cortex, thalamus and cingulum in rats that displayed seizures but not in those rats exposed to GB that did not seize. Rats exposed to 1.0 LD50 GB (with ATR, 2-PAM and DZP treatment) lost significant body weight relative to their pre-exposure (base) body weight. Rats that displayed seizures had a greater reduction in body weight in response to GB exposure than did those that did not display seizures. Motor deficits were observed following GB exposure in rats that displayed seizures. In a large arena open field test, rats that received GB and displayed seizures had reduced locomotor and exploratory activity indicated by reduced distance travelled and reduced speed of travel. Data analysis to determine motor coordination on a balance beam and home cage motor activity is in progress.

Although the rat model in which we give ATR and 2PAM 1 min after seizure onset was useful for comparing gene changes in rats exposed to GB that seize with those in rats that do not seize (since 50% seize and 50% do not seize; see Spradling et al. abstract), this model is limited for drug evaluation studies in that it only gives us 50% of the population in which to evaluate drug treatments. The soman model that we previously developed in which we give HI-6 pretreatment prior to exposure results in 95% survival with 90% displaying seizure and may be more useful for initial drug assessments to down-select drug treatments for further evaluation in the sarin model.

Estrogen and non-feminizing estrogen analogues have anticonvulsant and neuroprotectant effects against nerve agent exposure.

Lucille A. Lumley1, Marcio D. Furtado2, Christopher L. Robison1, Theresa M. Ward1, Jim Simpkins3, Stephen P. Estes1, Josh Kraft1, Debra L. Yourick2, Tsung-Ming Shih1, George A. Saviolakis2. 1US Army Medical Research Institute of Chemical Defense, Aberdeen Proving Ground, MD, USA; 2Walter Reed Army Institute of Research, Silver Spring, MD, USA 3University of North Texas Health Science Center, Fort Worth, TX, USA

Chemical warfare nerve agents are toxic organophosphorus compounds that irreversibly inhibit acetylcholinesterase, leading to accumulation of acetylcholine at peripheral and central synapses. One of the most harmful manifestations of the ensuing cholinergic intoxication and secondary responses is prolonged seizures that can lead to extensive brain pathology. Although current treatments for nerve agent toxicity promote survival, they also have unwanted side effects, have a narrow window of opportunity and are not fully neuroprotective. There is a need to identify adjunct therapeutics to reduce or prevent brain damage and performance deficits subsequent to nerve agent-induced seizures. We implemented a rat model of VX and soman (GD) toxicity to screen compounds for functional neuroprotection against nerve agents. The steroid hormone 17β-estradiol has been reported to have potent neuroprotective activity in a variety of in vivo and in vitro models, including ischemia and excitotoxicity. More recently, non-feminizing estrogen analogues have been evaluated for their neuroprotective potential. We evaluated 17β-estradiol and estrogen analogues for their protective efficacy against toxic doses of VX or GD using EEG, neuropathology and behavioral assessments as endpoints. Male rats pretreated with 17β-estradiol (0.1 mg/kg, sc) were exposed to 1.6 LD50 VX 30 min later, followed by a standard treatment consisting of atropine sulfate (ATR; 2 mg/kg, im), the oxime 2-PAM (25 mg/kg, im) and the anticonvulsant diazepam (DZP; 10 mg/kg, sc). Rats pretreated with 17β-estradiol experienced shorter periods of seizures and fewer rats displayed seizures compared with VX-exposed rats that did not receive

17β-estradiol. Rats pretreated with 17β-estradiol also had reduced brain pathology in the hippocampus, amygdala, piriform cortex, entorhinal cortex, cingulum and thalamus, demonstrated by using silver stain to label neuronal tract degeneration. Similar findings were observed in rats pretreated with 17β-estradiol (0, 0.1, 0.3, 1.0 mg/kg, sc) or the non-feminizing estrogen analogue ZYC-3 (0.1 mg/kg, sc) prior to exposure to 1.0 LD50 GD and treatment with the oxime HI-6 (125 mg/kg, ip), ATR (2 mg/kg, im) and DZP (10 mg/kg, sc). These findings show that estrogen compounds as adjunct therapy to atropine, an oxime and diazepam treatment reduce seizures and brain pathology in nerve agent-exposed rats to a greater extent than treatment with atropine, an oxime and diazepam.

Anticonvulsant effects of the neurosteroid pregnanolone against nerve agent-induced toxicity.

Lucille A. Lumley1, Mark C. Moffett1, Theresa M. Ward1, Stephen P. Estes1, Marcio D. Furtado2, Kristen L. Kamberger1, Julia E. Schwartz1, Mark K. Schultz1, Michael F. Stone1, George A. Saviolakis2. 1US Army Medical Research Institute of Chemical Defense, Aberdeen Proving Ground, MD, USA; 2Walter Reed Army Institute of Research, Silver Spring, MD, USA

The neuroactive steroid pregnanolone is a positive allosteric modulator of GABAA receptors with sedative, anxiolytic and anticonvulsant properties. Neuroactive steroids have anticonvulsant and neuroprotective properties in animal models of excitotoxicity. We evaluated whether treatment with pregnanolone protected against exposure to a toxic dose of soman (GD). Soman is a chemical warfare nerve agent that irreversibly inhibits acetylcholinesterase, leading to accumulation of acetylcholine at peripheral and central synapses. One of the most harmful manifestations of the ensuing cholinergic intoxication and secondary responses is prolonged seizures that can lead to extensive brain pathology. Although current treatments for nerve agent toxicity promote survival, they also have unwanted side effects, have a narrow window of opportunity and are not fully neuroprotective. There is a need to identify adjunct therapeutics to reduce or prevent brain damage and performance deficits subsequent to nerve agent-induced seizures.
In this pilot study, we evaluated whether treatment with pregnanolone (PREG; 4 mg/kg, iv) protects against exposure to 1.0 LD50 GD using endpoints of EEG, neuroanatomy and behavioral assessments. Male rats were pretreated with the cholinesterase reactivating oxime HI-6 (125 mg/kg, ip) 30 min prior to exposure to 1.0 LD50 GD (sc). One minute after exposure, rats were treated with atropine sulfate (ATR; 2 mg/kg, im) to prevent respiratory failure. One group of rats was treated with PREG (4 mg/kg, iv) immediately prior to exposure to GD. Another group of rats received PREG, diazepam (DZP; 10 mg/kg, sc), or a combination of PREG and DZP 30 min after seizure onset. Control rats received an equivalent volume of HI-6, saline, ATR, and DZP (and/or PREG), but were not exposed to GD. All rats that received PREG (in both groups) survived, while75% of rats that received HI-6, ATR, and DZP survived 24 hr and only 50% survived 48 hr post-exposure to GD. Pretreatment with PREG immediately prior to exposure to GD prevented seizure onset. This dose of PREG sedated the rats such that toxic signs were not observed in rats pretreated with PREG; the sedative effects of PREG dissipated within 3 hours. Rats pretreated with PREG (no seizure) tended to have more exploratory activity and rearing behavior in an open field test tested conducted two days after exposure, relative to those treated with vehicle prior to GD exposure (seizure). Rats pretreated with PREG also tended to perform better on a rotarod when tested three days after exposure.
Neuropathology findings are in progress and will be presented. Further studies are ongoing for a complete evaluation of the salutary effects of PREG on survival and seizures and to further compare combination treatments of DZP with PREG. These preliminary findings show that pretreatment with the positive allosteric modulator of GABAA receptors prevents mortality and has anticonvulsant effects against the nerve agent GD. Further studies are in progress to evaluate these effects of PREG.

Spectral Evaluation and Therapeutic Approaches to Behavioral and Electrographic Seizures after Exposure to the Organophosphorus Compound Soman.

S.D. Lichtenstein1, M.A. Furtado1, C. Robison2, L.A. Lumley2, T. Ward2, S. Estes2, B.D. Litwack1, K. Clements1 and D.L. Yourick1. 1Walter Reed Army Institute of Research, Silver Spring, MD, 2 U.S. Army Medical Research Institute of Chemical Defense (USAMRICD), Aberdeen Proving Ground, MD.

The threat of exposure to organophosphorus (OP) nerve agents exists on the battlefield, as a result of terrorism, and as part of current demilitarization efforts. Control of seizures resulting from OP exposure and means to mitigate central nervous system damage continue to be major military and civilian research goals. Soman exposure induces status epilepticus (SE), through magnification of cholinergic drive followed by excitatory amino-acid-induced brain injury.
N-Acetyl-β-aspartylglutamate (β-NAAG) is a potential neuroprotectant since efficacy has been shown against hypoxia- and NMDA-induced injury in vitro and ischemic spinal cord injury in vivo. This protection is likely due to low potency NMDA-agonist activity turned antagonist activity when Glu concentrations are high. Antioxidants such as phenyl t-butyl nitrone (PBN) have also been suggested as therapeutic intervention for oxidant damage as a consequence of soman-induced injury. Male rats were pretreated with the oxime HI-6 (125 mg/kg, i.p.) 30 min before the injection of soman (110 µg/kg, s.c.). One min after soman exposure, rats were injected with atropine SO4 (2 mg/kg, i.m.). At 30 min post soman exposure, diazepam (DZP, 10 mg/kg, s.c.) was injected for treatment of SE. Following the injection of DZP, a group of animals (n=13) received β-NAAG (4 and 8 µmols, i.c.v.) or its vehicle. PBN (75 mg/kg) was also tested in the same model of soman exposure utilizing

identical therapeutics. Fifteen days after exposure all animals were euthanized and their brains removed. Through the use of a customized Matlab program (Mathworks, Vers. 7), time spent in electrographic seizure and alteration in the EEG power spectra were evaluated. A strong correlation was found between time spent in seizures during the 1st day and brain damage quantified by silver staining. Additionally, the magnitude of the power spectra on the delta band remained increased in rats that had SE. Unexpectedly, PBN-treated rats spent more time in seizures than controls, suggesting a pro-convulsive effect of this compound. During the 1st day post exposure β-NAAG-treated rats (8 μmols) had a reduction in the power spectra on the delta band as well as a reduction in electrographic seizure activity and time spent in seizure compared to controls. Spontaneous recurrent seizures (SRS) were detected in both control and β-NAAG-treated rats with no statistical difference between groups. There was a strong correlation between time spent in seizure 24 hr after exposure and the number of SRS. Despite the significant reduction in seizure activity in the β-NAAG group, animals still showed marked brain damage. These and other data identify the continuous seizure activity, which persists even after the injection of DZP and neuroprotectant, as the main cause of SRS and neuropathology. Repeated treatment with anticonvulsants/neuroprotectiants may be needed to avoid OP neuroexcitotoxicity.

This work was supported by the U.S. Army Medical Research and Materiel Command and the Defense Threat Reduction Agency under Grants # 1.L0003_05_WR_C, 1.E0052_07_WR_C and previously funded grants from these sources.

Behavioral and Neuropathologic Outcomes after Ifenprodil Treatment in Soman-exposed Rats

Seth T. Fairfax, Scott Cohn, Chris Robison, Daniel Nagode, Lawrence Tong, Spencer Lichtenstein, Benjamin Litwack, Jamie Waterhouse,
Madineh Sedigh-Sarvestani, Marcio Furtado, Lucille Lumley and Debra Yourick. Division of Research, Marketing, and Policy Development, Walter Reed Army Institute of Research, Silver Spring, MD. U.S. Army Medical Research Institute of Chemical Defense, Aberdeen Proving Ground, MD

Soman, an organophosphate acetylcholinesterase inhibitor, is highly damaging to cells in the central nervous system and causes a spectrum of damage including convulsions, seizures and death. Following soman exposure, the resulting status epilepticus (SE) leads to neuronal damage and loss in numerous brain regions. Reduction of convulsions and intervention via excitatory amino acid mechanisms of neuronal injury may reduce neurotoxicity and preserve behavioral function. The NR2B-selective antagonist ifenprodil has been shown to provide neuroprotection in various models of injury including ischemic insults and kindling acquisition. This study sought to determine whether ifenprodil produces a significant neuroprotective effect as well as examine the subsequent motor performance, coordination and orientation ability, determined by the Morris water maze test.

In the present study, rats were pretreated with the oxime HI-6 (125 mg/kg, i.p.). Thirty minutes after oxime administration, soman (1.0 x LD50) was delivered subcutaneously followed by atropine SO4 (2 mg/kg, i.m.) 1 min later. Diazepam (10 mg/kg, i.p.), along with ifenprodil (10 or 20 mg/kg, i.p.) or an isovolemic sterile water control, was administered 30 minutes after soman administration to reduce the number and severity of seizures, overall neurotoxicity and lethal outcomes.

Following a 7-day stabilization period, the rats underwent 5 days of Morris water maze testing. Animals performed one trial from the north, south, east, and west pool coordinates on each day of testing. The three parameters measured were mean velocity, distance swam, and latency to reach the platform. Outcome variables represent the mean value from the four trials on a respective day of testing. All groups demonstrated an improvement in performance by significantly decreasing the distance swam and the latency in reaching the platform. In general, no significant differences were found between groups.

At 14 days post-exposure, rats were anesthetized and perfused with 100 mL of cold 0.1 M phosphate buffer (pH 7.4) and 400 mL 4% paraformaldehyde. Brains were removed, prepared and stained with silver nitrate for fiber degeneration. Brains were then qualitatively analyzed for damage in six regions: hippocampus, thalamus, amygdala, piriform cortex, cortex and fiber tracts.

In the current rat model of soman exposure, there is little hippocampal fiber degeneration noted. Tests assessing emotional responsiveness may be a more distinguishing measure for behavioral function in this soman exposure model. These conclusions are warranted on the basis of considerable damage to amygdala and piriform cortex of soman-exposed rat brains.

This work was supported by the U.S. Army Medical Research and Materiel Command and the Defense Threat Reduction Agency under Grant# 1.L0003_05_WR_C and previously funded grants from these sources.

Abstract, Annual meeting of Society for Neuroscience, Washington, DC, 2008.

Effects of pentoxifylline in seizures induced by organophosphorus compounds in Sprague-Dawley rats.

AUTHORS. *M. D. FURTADO1, L. LUMLEY2, M. SEDIGH-SARVESTANI1, K. E. CLEMENTS1, S. FAIRFAX1, S. LICHTENSTEIN1, M. ADDIS1, C. ROBISON2, D. L. YOURICK1; 1Headquarters, USAMRMC/WRAIR, Silver Spring, MD; 2U.S. Army Med. Res. Inst. of Chem. Def., Aberdeen Proving Ground, MD.

The control of seizures induced by organophosphorus (OP) exposure and means to reduce brain damage continue to be major military and civilian research goals. OP exposure causes hyperactivation of the cholinergic system due to inactivation of acetylcholinesterase (AChE) causing an increase in acetylcholine in central and peripheral nervous systems. Antioxidants such as Pentoxifylline (PTX) have been suggested as a therapeutic intervention for the oxidative damage of soman-induced injury. Male Sprague-Dawley rats were implanted with telemetry transmitters which recorded cortical EEG, motor activity and temperature 24 hours/day immediately after surgery. After a minimum surgical recovery of 7 days, rats were pretreated with the oxime HI-6 (125 mg/kg, i.p.) 30 min prior to soman injection (110 µg/kg, s.c.). Rats were injected with atropine SO4 (2 mg/kg, i.m.) one min after soman exposure. Diazepam (DZP, 10 mg/kg, s.c.) was injected for treatment of SE at 30 min post soman exposure along with PTX (60 mg/kg, i.p.) or vehicle. Animals were euthanized 24 or 72 hours after exposure and their brains were removed. The brains are processed with Nissl, Silver and Fluoro-Jade staining. Time spent in electrographic seizures was estimated through the use of a customized Matlab program (Mathworks, Vers. 7) and visual screening. The time spent in seizures was not significantly different between PTX treated rats and their respective controls. Core body temperature decreased in rats exposed to soman and returned to basal levels 24 hours after exposure. Future experiments are planned to test a range of doses of PTX. Also, neuropathological assessments are performed to quantify nerve fiber degeneration and the number of degenerating neurons.

12) *SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES* **Include dates, names and locations of seminars.**

NATIONAL RESEARCH COUNCIL ASSOCIATESHIP PROGRAMS STAFF VISIT. Walter Reed Army Institute of Research Bldg. 503, Room 1W81. Thursday, June 11, 2009. Presentation: Spontaneous recurrent seizures after status epilepticus induced by soman in Sprague-Dawley rats.

13) *PROFESSIONAL AWARDS RECEIVED DURING TENURE*

Appreciation for the help and support for the Science & Engineering Apprentice Program (SEAP) and College Qualified Leaders (CQL) program, WRAIR, 2007.

14) *POST-TENURE POSITION TITLE*

Neuroscientist.

15) *POST-TENURE ORGANIZATION* **Provide name and address of organization.**

Walter Reed Army Institute of Research. 503 Robert Grant Ave. Silver Spring, MD 20910. Contractor - Clinical Research Management, Inc.

16) *POST-TENURE POSITION STATUS / CATEGORY* **Please indicate only one.**

- ☐ Remain at Host Agency as Permanent Employee
- ☒ Remain at Host Agency as Contract/Temporary Employee
  - **Abbreviate Host Laboratory/Center** WRAIR
- ☐ Research Position at Another US Government Laboratory
- ☐ Administrative Position at US Government Laboratory
- ☐ Research Position at Foreign Government Laboratory
- ☐ Research/Teaching at US College/University
- ☐ Research/Teaching at Foreign College/University
- ☐ Research/Administration in Industry
- ☐ Research/Administration in Non-Profit Organization
- ☐ Postdoctoral Research
- ☐ Self Employed
- ☐ Other: **specify** _____

17) *APPRAISAL OF RESEARCH ASSOCIATESHIP PROGRAM*

On a scale of 1 – 10 (poor - excellent), please rate the following:

SHORT TERM VALUE

7 Development of knowledge, skills, and research productivity

Comments

The laboratory offered the chance to improve my background on neuroprotection. Previously know technical skills were improved and few other methodologies were added to my background. Research productivity was good, and would be better with more balance between experiments and data analysis in terms of time.

LONG TERM VALUE

10 How the National Academies Associateship award affected your career to date

Comments

The award and the chalenge to perform studies in the field of neuroprotection and chemically induced seizures was a unique experience.

LAB SUPPORT

7 Quality of support--equipment, funding, orientation, safety and health guidelines, etc.

Comments

Both laboratory equipment, funding, orientation, safety and health guidelines attended the expectations. However, the delay when ordering supplies/equipment/sofware due to internal regulations was a limiting factor.

ADVISER/MENTOR SUPPORT

8 Quality of mentoring from the Lab NRC Adviser (USMA Mentor, if applicable)

Comments

The NRC adviser has an impressive scientific experience. Periodic meetings were done for data review and discussions. However, more priority should be given for publication in peer reviewed journals.

LPR SUPPORT

10 Quality administrative support from the LPR

Comments

The NRC Program Representative always gave the necessary orientation.

NRC SUPPORT

8 Quality of administrative support from the NRC

Comments

Applications, inquiries and awarded related issues had and excelent administrative support. Travel related issues such as advance deposit and reimbursement had delays caused by financial department errors.

18) *PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT.*

1. Continue promoting at least one NRC visit staff a year. 2. Allow electronic submission, processing and approval of forms in order to reduce the chance of failures and decrease the processing time. 3. Electronic submission of travel expense reports. 4. Require at least one peer reviewed publication per year of tenure.

b) Books, book chapters, other publications

c) Manuscripts in preparation, manuscripts submitted

Hooper, J.W., Ferro A.M., Golden, J.W., Silvera, P., Dudek, J., Alterson, K., Custer, M., Rivers, B., Morris, J., Owens, G., Smith, J.F. and Kamrud, K.I. Molecular Smallpox Vaccine Delivered by Alphavirus Replicons Elicits Protective Immunity in Mice and Non-human Primates. Manuscript in submission.

Golden, J.W., Fisher, R.W., and Hooper, J.W. Antibodies elicited by DNA vaccination are sufficient for protection against orthopoxvirus infections. Manuscript in preparation.

10) *PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NATIONAL ACADEMIES ASSOCIATESHIP RESEARCH*

Provide titles, inventors, and dates of applications.

Hooper. J.W. and Golden, J.W. "Modification of L1R gene to Improve Neutralizing Antibody Responses Elicited by Molecular Smallpox Vaccines." U.S. Patent Application filed 9 Jul 09.

11) *PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES*

Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.

International

Golden, J.W. and Hooper, J.W. Targeting the Vaccinia Virus L1 Protein to the Cell Surface Enhances Production of Neutralizing Antibodies. International Congress of Virology. 2008. Poster Presentation.

Golden, J.W. and Hooper, J.W. Heterogeneity in A33 Epitope Affects Cross Protective Efficacy of Smallpox DNA Vaccine. The 3rd International DNA Vaccine Conference. 2007. Poster Presentation.

Domestic

Anti-orthopoxvirus therapeutics: Targeting the L1 molecule. Defense Advanced Research Projects Agency (DARPA) Protein Design Processes Meeting. Seattle, WA. September 2008. Oral Presentation.

12) *SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES* **Include dates, names and locations of seminars.**

13) *PROFESSIONAL AWARDS RECEIVED DURING TENURE*

14) *POST-TENURE POSITION TITLE*

Reseach microbiologist/Principal investigator

15) *POST-TENURE ORGANIZATION* **Provide name and address of organization.**

U.S. Army, USAMRIID, 1425 Porter St. Ft. Detrick, MD 21702

16) *POST-TENURE POSITION STATUS / CATEGORY* **Please indicate only one.**

- ☐ Remain at Host Agency as Permanent Employee
- ☒ Remain at Host Agency as Contract/Temporary Employee
  Abbreviate Host Laboratory/Center **USAMRIID**
- ☐ Research Position at Another US Government Laboratory
- ☐ Administrative Position at US Government Laboratory
- ☐ Research Position at Foreign Government Laboratory
- ☐ Research/Teaching at US College/University
- ☐ Research/Teaching at Foreign College/University
- ☐ Research/Administration in Industry
- ☐ Research/Administration in Non-Profit Organization
- ☐ Postdoctoral Research
- ☐ Self Employed
- ☐ Other: **specify** _____

17) *APPRAISAL OF RESEARCH ASSOCIATESHIP PROGRAM*
On a scale of 1 – 10 (poor - excellent), please rate the following:

SHORT TERM VALUE

☐ Development of knowledge, skills, and research productivity
Comments
9

LONG TERM VALUE

☐ How the National Academies Associateship award affected your career to date
Comments
9

LAB SUPPORT

☐ Quality of support--equipment, funding, orientation, safety and health guidelines, etc.
Comments
6: Funding at USAMRIID is complicated and based on an annual competative granting process that makes it uncertain if funding for a particular project (such as an NRC project) will be available. This makes it difficult on one whose fellowship needs to last at least three years to be competitive in the "real-world". It puts additional strains on the fellow as they need to worry about securing funding annually and MAY make it difficult to stay focused on the research proposed by the NRC fellow.

ADVISER/MENTOR SUPPORT

☐ Quality of mentoring from the Lab NRC Adviser (USMA Mentor, if applicable)

Comments
9

LPR SUPPORT

☐ Quality administrative support from the LPR
Comments
10: Brad Stiles, 6: Sina Bavari

NRC SUPPORT

☐ Quality of administrative support from the NRC
Comments
9

18) *PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT.*

Make it clear to fellows that it is critical they talk with advisors on how long funding will last and what happens if that funding ends before the anticipated research is complete. Also, the NRC should ensure that post-docs are doing the research outlined in their proposals and that they do not become some psudo-technician exprected to do the work of the PIs laboratory-This was a problem that occurred in certain USAMRIID labs (Chris Curtis and Steven Bradfuete were the fellows). Additionally, the NRC should have guidelines for picking who can be an advisor, i.e. a PI with (for example) 5 years of experience and not a newly converted person who has never had a lab. The NRC should also find a means to encourage publications.

US Postal Service mailing address
Research Associateship Programs
The National Academies
500 Fifth Street NW
Washington, DC 20001

THIS FORM SHOULD BE E-MAILED
directly to your NRC coordinator
website
www.national-academies.org/rap

Express Delivery address
Research Associateship Programs
The National Academies
2001 Wisconsin Avenue, NW [GR 322A]
Washington, DC 20007

Provide titles, inventors, and dates of applications.

None

11) *PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES*

Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.

International

Domestic

1. B. Keyser, D. Andres, B. Benton, R. Ray. Small interfering RNA (siRNA) suppresses the Fas Response Amplification loop in sulfur mustard (SM)-exposed normal human bronchial/tracheal epilthelial cells (NHBE). Abstract. FASEB, New Orleanse, LA, 2009

2. R. Ray, B. Keyser, D. Andres, S. Hauck, B. Benton, C. Carpin, A.Daher, C. Simbulan-Rosenthal, D. Rosenthal. Normal Human bronchial/tracheal epithelial (BEC) are more sensitive than small airway epithelial cells (SAEC) to sulfur mustard-induced apoptosis apparently due to a Fas (death receptor) response amplification loop. Abstract. FASEB, San Diego, CA, 22:648.6, also at Bioscience Review 2008, Hunt Valley, MD.

3. B. Keyser, D. Andres, B. Benton, R. Ray. Fas targeted siRNA markedly attenuates sulfur mustard-induced apoptosis in human airway epithelial cells. Abstract. FASEB, San Diego, CA, 22:1140.1, also at Bioscience Review 2008, Hunt Valley, MD.

4. B. Keyser, D. Andres, C. Carpin, B. Benton, R. Ray. Fas receptors mediate sulfur mustard-induced apoptosis in human epidermal keratinocytes and airway epithelial cells. Abstract. FASEB, Washington D.C., 21:728.9, May 2007.

5. R. Ray, B. Benton, B. Keyser, C. Carpin, D. Rosenthal. Sulfur mustardinduced-apoptosis in human airway epithelial cells appears to be via the death receptor (Fas) pathway. Abstract. FASEB, Washington D.C., 21:497.8, May 2007.

6. R. Ray, B. Benton, C. Carpin, S. Hauck, B. Keyser, D. Rosenthal. Protection against the vesicant chemical warfare agent sulfur mustard: Therapeutics utilizing apoptosis inhibitors. Abstract. 25th Army Science Conference, Orlando, FL, FP-14, Nov 2006.

12) *SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES* **Include dates, names and locations of seminars.**

1. August 13, 2009 "Vesicant Countermeasure via Fas Intervention" USAMRICD
2. July 27, 2009 "Apoptosis, Calcium Channels and Pain" USAMRICD
3. Febuary 10, 2009 "Fas Receptor Antagonism via siRNA Markedly Attenuates Sulfur Mustard Induced Apoptosis in Normal Human Airway Epithelial Cells" St. Jude Memphis, TN

13) *PROFESSIONAL AWARDS RECEIVED DURING TENURE*

USAMRICD Commander's Award for Research Excellence 2007

14) *POST-TENURE POSITION / JOB TITLE*

Senior Research Scientist

15) *NAME AND ADDRESS OF POST-TENURE POSITION / JOB 0RGANIZATION*

3100 Ricketts Point Road APG, MD 21010

16) *POST-TENURE POSITION STATUS / CATEGORY* **Please indicate only one.**

- ☐ Remain at Host Agency as Permanent Employee
- ☒ Remain at Host Agency as Contract/Temporary Employee
  - **Abbreviate Host Laboratory/Center** **USAMRICD**
- ☐ Research Position at Another US Government Laboratory
- ☐ Administrative Position at US Government Laboratory
- ☐ Research Position at Foreign Government Laboratory
- ☐ Research/Teaching at US College/University
- ☐ Research/Teaching at Foreign College/University
- ☐ Research/Administration in Industry
- ☐ Research/Administration in Non-Profit Organization
- ☐ Postdoctoral Research
- ☐ Self Employed
- ☐ Other: **specify** _____

17) *APPRAISAL OF RESEARCH ASSOCIATESHIP PROGRAM*

On a scale of 1 – 10 (poor - excellent), please rate the following:

SHORT TERM VALUE

8 Development of knowledge, skills, and research productivity
Comments

LONG TERM VALUE

7 How the NRC Associateship award affected your career to date
Comments

LAB SUPPORT

9 Quality of support from the Laboratory--equipment, funding, orientation, safety and health guidelines, etc.
Comments

ADVISER/MENTOR SUPPORT

10 Quality of mentoring from the Laboratory NRC Adviser (USMA Mentor, if applicable)
Comments

My mentor has been instrumental in training me into becoming an independent scientist. His wisdom, insight, patience and kindness have helped me immensely.

LPR SUPPORT

9 Quality of administrative support from the Laboratory (e.g., NIST) NRC Program Representative (LPR)
Comments

NRC SUPPORT

7 Quality of administrative support (applications, inquiries, post-review, award-related, travel, etc.) from the NRC
Comments

Improve communication between NRC and the fellows - some way to let the assiocate know that NRC received travel documents, change of address, renewal forms, etc. An auto generated email would suffice.

18) *PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT.*

Mail & Delivery Address

It is NOT necessary to mail the original.
The National Academies
NRC Research Associateship Programs
500 Fifth Street NW, #568
Washington, DC 20001

This form SHOULD be E-MAILED directly to the NRC Coordinator.

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Rev. Jan. 2008

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ID#

CC#

2. Nick Steers, Dmitry J. Liepinsh, Robert Schwenk and Urszula Krzych. The involvement of TAP in protective immunity to malaria: the induction of liver-stage antigen-specific CD8 T cell responses by radiation-attenuated Plasmodium berghei sporozoites is TAP-independent but the recall of the effector CD8 T cells during malaria infection is TAP-dependent (Manuscript in preparation).

10) *PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NATIONAL ACADEMIES ASSOCIATESHIP RESEARCH*
Provide titles, inventors, and dates of applications.

11) *PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES*
Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.

International

Domestic

1. Dmitry J. Liepinsh, Nick Steers, Robert J. Schwenk and Urszula KrzychThe involvement of TAP in protective immunity to malaria: the induction of liver-stage antigen-specific CD8 T cell responses by radiation-attenuated P.berghei sporozoites is TAP-independent but the recall of the effector CD8 T cells during malaria infection is TAP-dependent. 11th Woods Hole Immunoparasitology Meeting. Woods Hole, MA (April 2007). Poster presentation.

2. Liepinsh D.J., Steers N, Schwenk R.J., and Krzych U. Sterile protection against malaria infection requires TAP in spite of completely operative TAP-independent vacuolar cross-presentation pathway. 94th Annual Meeting of the American Association of Immunologists. Miami Beach, FL (May 2007). Poster presentation. Abstract published in The Journal of Immunology, 2007, 178: B40. http://www.jimmunol.org/cgi/content/meeting_abstract/178/MeetingAbstracts/LB8-c.

3. Dmitry J. Liepinsh, Nick Steers, Robert J. Schwenk and Urszula Krzych. TAP-independent cross-presentation pathway is not sufficient to confer sterile protection in Pb g-spz immunization model. 56th Annual Meeting of the American Society of Tropical Medicine and Hygiene. Philadelphia, PA. (November 2007). Poster Presentation.

12) *SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES* **Include dates, names and locations of seminars.**

13) *PROFESSIONAL AWARDS RECEIVED DURING TENURE*

14) *POST-TENURE POSITION TITLE*

Physician-in-training (Internal Medicine Residency)

15) *POST-TENURE ORGANIZATION* **Provide name and address of organization.**

Greater Baltimore Medical Center. 6701 N. Charles Street, Baltimore, MD 21204

16) *POST-TENURE POSITION STATUS / CATEGORY* **Please indicate only one.**

- ☐ Remain at Host Agency as Permanent Employee
- ☐ Remain at Host Agency as Contract/Temporary Employee
  Abbreviate Host Laboratory/Center _____
- ☐ Research Position at Another US Government Laboratory
- ☐ Administrative Position at US Government Laboratory
- ☐ Research Position at Foreign Government Laboratory
- ☐ Research/Teaching at US College/University
- ☐ Research/Teaching at Foreign College/University
- ☐ Research/Administration in Industry
- ☐ Research/Administration in Non-Profit Organization
- ☐ Postdoctoral Research
- ☐ Self Employed
- ☒ Other: **specify** **Physician**

17) *APPRAISAL OF RESEARCH ASSOCIATESHIP PROGRAM*
On a scale of 1 – 10 (poor - excellent), please rate the following:

SHORT TERM VALUE

8 Development of knowledge, skills, and research productivity
Comments

LONG TERM VALUE

7 How the National Academies Associateship award affected your career to date
Comments

LAB SUPPORT

8 Quality of support--equipment, funding, orientation, safety and health guidelines, etc.
Comments
Very often the equipment needed to conduct the study was located in other laboratories which was ok but somewhat inconvenient.

ADVISER/MENTOR SUPPORT

8 Quality of mentoring from the Lab NRC Adviser (USMA Mentor, if applicable)

Comments

LPR SUPPORT

8 Quality administrative support from the LPR
Comments

NRC SUPPORT

8 Quality of administrative support from the NRC

Comments

18) *PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT.*

Medical insurance leaves much to be desired. It has high out-of-pocket deductible and is restrictive in many ways. I am sure it would be greatly appreciated by new NRC associates if the NRC stuff could improve health coverage for the associates and their families. At least adding more expensive insurance (for which an associate shares the cost) would be a reasonable additional option. The absence of dental insurance does not add anything good to the tenure experience. Also, It would be nice to have bigger stipend increases after transition to the next year.

11) *PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES*

Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.

International

Domestic

Molecular Modeling Studies on the Binding of 2-PAM and MMB4 to Nerve-agent-Inhibited Human Acetylcholinesterase, Yun Ling, Nagarajan Pattabiraman, Chunyuan Luo, Carolyn Chambers, and Ashima Saxena. Bioscience Review Meeting, June 2008, Hunt Valley, MD

Organophosphorus compounds (OP), such as sarin (Fig. 1), soman (Fig. 1), GF, VX, VR, and tabun pose a lethal threat to humans by inhibiting acetylcholinesterase (AChE), a key enzyme in the nervous system. One of the antidotes involves oximes, a group of organic molecules, which can reactivate OP-inhibited AChE. 2-PAM (Fig.1), a mono-pyridinium oxime, was first adopted by the U.S. Army in the 1950's. However, the efficacy of 2-PAM is very limited against poisoning by certain nerve agents such as soman and cyclosarin. Recently, a new symmetric bispyridinium oxime MMB4 (Fig.1) was selected as a broad-spectrum candidate for the next generation antidote. MMB4 was shown to be a significantly better reactivator of human (Hu) AChE inhibited by soman, sarin, GF, VX, VR, and tabun compared to 2-PAM in our laboratory. In order to understand the differences in the activities of these two oximes, we used computer modeling to simulate the interactions between the oximes (2-PAM and MMB4) and the OP (sarin and soman)-inhibited Hu AChE before nucleophilic attack of the phosphate attached to S203. All these models were subjected to 1 nano-second MD simulations. Interaction energy calculations revealed that MMB4 formed stronger interactions with soman- and sarin-inhibited enzyme than did 2-PAM. A closer structural analysis of the binding pocket showed that W286, located at the peripheral anionic site of Hu AChE, may be the key residue that contributed to the better interaction by forming a ring-ring stacking interaction with the 2nd pyridinium ring of MMB4. Further molecular dynamics simulations and energy calculations on the W286A and W286F mutants show that W286 was indeed one of the key residues in stabilizing the oxime molecule in the binding pocket. This result agrees with the data from the mutagenesis studies conducted in our group.

12) *SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES* **Include dates, names and locations of seminars.**

13) *PROFESSIONAL AWARDS RECEIVED DURING TENURE*

14) *POST-TENURE POSITION / JOB TITLE*

15) *NAME AND ADDRESS OF POST-TENURE POSITION / JOB 0RGANIZATION*

16) *POST-TENURE POSITION STATUS / CATEGORY* **Please indicate only one.**

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- ☐ Postdoctoral Research
- ☐ Self Employed
- ☐ Other: **specify** _____

17) *APPRAISAL OF RESEARCH ASSOCIATESHIP PROGRAM*

On a scale of 1 – 10 (poor - excellent), please rate the following:

SHORT TERM VALUE

10 Development of knowledge, skills, and research productivity

Comments

I was able to gain more experience in molecualr biology, cell culture and lab automation.

LONG TERM VALUE

10 How the NRC Associateship award affected your career to date

Comments

LAB SUPPORT

☐ Quality of support from the Laboratory--equipment, funding, orientation, safety and health guidelines, etc.

Comments

ADVISER/MENTOR SUPPORT

☐ Quality of mentoring from the Laboratory NRC Adviser (USMA Mentor, if applicable)
Comments

LPR SUPPORT

☐ Quality of administrative support from the **L**aboratory (e.g., NIST) NRC **P**rogram **R**epresentative (LPR)
Comments

NRC SUPPORT

10 Quality of administrative support (applications, inquiries, post-review, award-related, travel, etc.) from the NRC
Comments
NRC staff have been very friendly and useful in provideing help on getting reimbursement, getting official documents and so on.

18) *PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT.*

Mail & Delivery Address

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500 Fifth Street NW, #568
Washington, DC 20001

ID# 0623010

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CC#

b) Books, book chapters, other publications

N/A

c) Manuscripts in preparation, manuscripts submitted

Patrick Mc Gann, Nikolich M.P., Bowden, R.A, Lindler, L.E., and Lathigra R. Growth kineties of Francisella species in a modified BHI broth. Submitted for publication November 2008, Journal of Microbiological Methods.

Patrick Mc Gann, Jones, M., Nikolich M.P., Bowden, R.A, Minoghue, T., Petersen, S., and Lathigra R. Transient changes in the global transcriptome of Francisella tularensis LVS and Schu S4 in response to pH change. Manuscript in Preparation.

Patrick Mc Gann, Jones, M., Nikolich M.P., Bowden, R.A, Minoghue, T., Petersen, S., and Lathigra R. Whole transcriptome analyses of Francisella tularensis LVS and Schu S4 response to Temperature change and Oxidative stress. Manuscript in Preparation.

Patrick Mc Gann, Jones, M., Nikolich M.P., Bowden, R.A, Minoghue, T., Petersen, S., and Lathigra R. Transcriptome analyses of Francisella tularensis LVS and Schu S4 during macrophage invasion. Manuscript in preparation

10 *PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM THE NRC ASSOCIATESHIP RESEARCH PROGRAM*

Provide titles, inventors, and dates of applications.

N/A

11) *PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES*

Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.

International

Domestic

P. McGann, M. Jones, T. Minogue, S. Peterson, M.J. Nikolich, and R. Lathigra. 2008. Transcriptome Response of Francisella tularensis to Temperature Change. Poster Presentation at ASM Biodefense, 2008.

12) *SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES* **Include dates, names and locations of seminars.**

N/A

13) *PROFESSIONAL AWARDS RECEIVED DURING TENURE*

N/A

14) *POST-TENURE POSITION / JOB TITLE*

Army Civilian Research Scientist

15) *NAME & ADDRESS OF POST-TENURE POSITION / JOB ORGANIZATION*

Walter Reed Army Institute of Research, Dept. of Bacterial & Rickettsial Diseases, Room 3A08, 503 Robert grant Avenue, Silver Spring, MD 20910.

16) *POST-TENURE POSITION STATUS / CATEGORY* **Please indicate only one.**

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- [x] Remain at Host Agency as Contract/Temporary Employee
  Abbreviate Host Laboratory/Center WRAIR
- [ ] Research Position at Another US Government Laboratory
- [ ] Administrative Position at US Government Laboratory
- [ ] Research Position at Foreign Government Laboratory
- [ ] Research/Teaching at US College/University
- [ ] Research/Teaching at Foreign College/University
- [ ] Research/Administration in Industry
- [ ] Research/Admin in Non-Profit Organization
- [ ] Postdoctoral Research
- [ ] Self Employed
- [ ] Other: specify _____

17) *APPRAISAL OF RESEARCH ASSOCIATESHIP PROGRAM*
On a scale of 1 – 10 (poor - excellent), please rate the following:

SHORT TERM VALUE

10 Development of knowledge, skills, and research productivity
Comments

LONG TERM VALUE

10 How the NRC Associateship award affected your career to date
Comments

The NRC Fellowship has been the most important career move for me to date, and has opened up a world of possibilities that were heretofore unimaginable.

LAB SUPPORT

8 Quality of support from the Laboratory--equipment, funding, orientation, safety and health guidelines, etc.
Comments

may aspects of my laboratory were exemplary, but in a sign of the difficult financial times, funding was limited and purchase of Capital equipment of high cost difficult

ADVISER/MENTOR SUPPORT

10 Quality of mentoring from the Laboratory NRC Adviser (USMA Mentor, if applicable)
Comments

Dr. Nikolich has been fantastic as a mentor and created a very favorable environment for work

LPR SUPPORT

10 Quality of administrative support from the Laboratory (e.g., NIST) NRC Program Representative (LPR)
Comments

Dr. Sara Rothman is an amazing person, and always had a friendly face and readily made time for discussions, both formal and informal.

NRC SUPPORT

10 Quality of administrative support (applications, inquiries, post-review, award-related, travel, etc.) from the NRC
Comments

Excellent support. A special mention for Peggy Wilson who went above and beyond to accommodate me with the many visa questions I had, and for the invaluable information provided

18) *PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT.*

Overall, the program was superb and I thoroughly enjoyed my tenure. I would suggest that foreign nationals be made aware of the numerous problems associated with working in sensitive areas, such as Biodefense. These caused me a lot of headaches and I was unaware of them when starting.

Mail & Delivery Address

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Washington, DC 20001

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ID# 0621750

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3. Peter Wipf, Tingting Mo, Steven J. Geib, Diana Caridha, Geoffrey S. Dow, Lucia Gerena, Norma Roncal and Erin E. Milner. Synthesis and biological evaluation of the first pentafluorosulfanyl analogs of mefloquine. Royal Society of Chemistry. Manuscript waiting on patent completion.

4. Charlotte A. Lanteri, Lucia Gerena, Montip Gettayacamin, William McCalmont, Erin Milner, Victor Melendez, Nicanor Obaldia III, Kirsten Smith, and Geoffrey S. Dow. In Vivo Antimalarial Efficacy and Partial Pharmacokinetic Properties of Alkylaminoquinolinyl Methanol Analogs of Mefloquine. Antimicrobial Agents and Chemotherapy. Manuscript waiting on WRAIR approval.

10) *PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH*
Provide titles, inventors, and dates of applications.

1. Docket No. WRAIR 09-19: Dow, Geoffrey S. (Contractor, Kootamiara, LLC); Milner, Erin (NRC Fellow); Geib, Steven J. and Mo, Tingting (Univ of Pittsburgh) "Synthesis and Biological Evaluation of the First Pentafluorosulfanyl Analogs of Mefloquine," rec'd 14 May 09.

2. U.S. Provisional Patent Application Number 61/093,560 was filed on September 2, 2008, "Next Generation Quinoline Methanols for Malaria and Other Indications," by Geoffrey S. Dow, William F. McCalmont, and Erin E. Milner. MRMC Docket No. WRAIR 08-39X.

11) *PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES*
Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.

International

Domestic

POSTER: Milner, E.; McCalmont, W.; Cobar, J.; Caridha, D.; Bhonsle, J.; Lanteri, C.; Melendez, V.; Dow, G., Malaria: Lead Optimization of Next Generation Quinoline Methanols. 235th National American Chemical Society Meeting, New Orleans, LA, April 2008.

POSTER: Jason Sousa, Erin Milner, Xiannu Jin, Michael Kozar, William McCalmont, Charlotte Lanteri, Constance Asher, Raul Olmeda, Dustin Carroll, Necole Reese, Lalaine Anova, Norma Roncal, Lucia Gerena, Nicanor Obaldia, Geoffrey Dow, and Victor Melendez. In Vitro and In Vivo Evaluations of New Quinoline Methanol Analogs of Mefloquine. 57th American Society of Tropical Medicine and Hygene Meeting. New Orleans, LA, December 2008.

POSTER: Cobar, J.; Milner, E.; Goodine, D.; Heady, T.; McCalmont, W.; Dow, G. Phototoxicity of 2-Substituted Quinoline Analogs. 40th Middle Atlantic Regional Meeting of the American Chemical Society, Queens, NY, May 2008.

12) *SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES* **Include dates, names and locations of seminars.**

13) *PROFESSIONAL AWARDS RECEIVED DURING TENURE*

14) *POST-TENURE POSITION / JOB TITLE*

Captain, US Army Medical Service Corps

15) *NAME AND ADDRESS OF POST-TENURE POSITION / JOB ORGANIZATION*

Walter Reed Army Institute of Research (first duty station)

16) *POST-TENURE POSITION STATUS / CATEGORY* **Please indicate only one.**

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- ☐ Research/Administration in Non-Profit Organization
- ☐ Postdoctoral Research
- ☐ Self Employed
- ☐ Other: **specify** _____

17) *APPRAISAL OF RESEARCH ASSOCIATESHIP PROGRAM*
On a scale of 1 – 10 (poor - excellent), please rate the following:

SHORT TERM VALUE

10 Development of knowledge, skills, and research productivity

Comments

Excellent opportunity. Made the most of it and cannot wait to recruit other NRC fellows.

LONG TERM VALUE

8 How the NRC Associateship award affected your career to date

Comments

It was an excellent transition between graduate school and being an Army officer.

LAB SUPPORT

10 Quality of support from the Laboratory--equipment, funding, orientation, safety and health guidelines, etc.

Comments

Excellent equipment, funding, etc.

ADVISER/MENTOR SUPPORT

10 Quality of mentoring from the Laboratory NRC Adviser (USMA Mentor, if applicable)

Comments

LTC Kozar provides support when needed but allows the fellow to work independently. He is encouraging while letting you run your own project(s) and laboratory.

LPR SUPPORT

10 Quality of administrative support from the Laboratory (e.g., NIST) NRC Program Representative (LPR)

Comments

Dr. Rothman provided me with a wonderful opportunity to be a member of the WRAIR Scientific Management Committee. This provided me the opportunity to meet leadership in headquarters and to observe a broad overview of the institute. I learned a great deal about MTAs, CRADAs, IAAs, etc. and it improved my grant writing knowledge.

NRC SUPPORT

3 Quality of administrative support (applications, inquiries, post-review, award-related, travel, etc.) from the NRC

Comments

Dr. Nyguist, Jason Thornhill, and Albert Llaguri are wonderful.

18) *PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT.*

Please provide a formal letter that states NRC associates are not supposed to pay full self employment taxes to the IRS.

Mail & Delivery Address

It is NOT necessary to mail the original.

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11) *PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES*

Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.

International

1) Yuki Murakami, Xi-Chun May Lu, Xiaofang Yang, Frank C. Tortella, and Guo Wei. Reduction of Brain Oxygen Tension Following Penetrating Ballistic-Like Brain Injury in Rats.
(Abstract) Clinically, brain tissue oxygen tension (PbtO2) is one of the most important parameters for evaluating severity of injury and the outcome of therapeutic intervention in patients having sustained a traumatic brain injury. To determine the status of cerebral oxygen level following a penetrating injury, we measured PbtO2 levels in an experimental model of penetrating ballistic-like brain injury (PBBI). Rats were anesthetized with isoflurane (2%) mixed in oxygen and air. The inhalational oxygen was maintained at 25-26% to minimize its interference on PbtO2. An oxygen probe was implanted along with a temperature probe into the brain near the core region of the injury (~2 mm lateral; 2.5 mm posterior to bregma and ~6 mm in depth) to record PbtO2 and brain temperature. The mean arterial blood pressure (MABP) was monitored by a femoral artery catheter and the body temperature was maintained at 37°C. Rats were subjected to a right frontal PBBI or sham surgery. All parameters were monitored continuously beginning at 15 min (baseline) prior to PBBI and ending at 150-min post PBBI. Within 5 min post injury, PbtO2was significantly reduced by ~40% in PBBI rats (16.9 mmHg ±4.0) as compared to sham rats (28.6 mmHg ± 6.2; mean ± SD, $p < 0.05$). This reduced PbtO2 was sustained for at least 150 min post PBBI. No significant differences in other physiological parameters, i.e. MABP, body or brain temperatures, were observed between PBBI and sham rats. In summary, our observations provide direct evidence of acute decreases in PbtO2 immediately after PBBI, indicating a metabolic disturbance in the peri-lesion regions of the injury. Further studies are underway to evaluate the time course of PbtO2 reduction and its effect on the surrounding brain areas. Collectively, these data will provide important information on the development of secondary injury associated with PBBI and help to further define a rationale therapeutic strategy to prevent PBBI induced reductions in PbtO2 and improve brain metabolic dysfunction. Neurotrauma, Santa Barbara, CA.

Domestic

N/A

12) *SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES* **Include dates, names and locations of seminars.**

N/A

13) *PROFESSIONAL AWARDS RECEIVED DURING TENURE*

N/A

14) *POST-TENURE POSITION / JOB TITLE*

Research assistant/Research resident

15) *NAME AND ADDRESS OF POST-TENURE POSITION / JOB 0RGANIZATION*

Human Health Sciences Kyoto University Graduate School of Medicine
54 Kawaharacho, Shogoin, Sakyo-ku, Kyoto 606-8507, JAPAN

16) *POST-TENURE POSITION STATUS / CATEGORY* **Please indicate only one.**

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- ☐ Research/Administration in Non-Profit Organization
- ☐ Postdoctoral Research
- ☐ Self Employed
- ☐ Other: **specify** _____

17) *APPRAISAL OF RESEARCH ASSOCIATESHIP PROGRAM*

On a scale of 1 – 10 (poor - excellent), please rate the following:

SHORT TERM VALUE

8 Development of knowledge, skills, and research productivity

Comments

Traumatic brain injury (TBI) is common injury and serious problem in clinical. I had some knowledge for neurodisease, but it was a really good opportunity to learn about TBI. I learned a lot of new skills for brain surgery and TBI model. Our TBI model is really novel and I guess if I wasn't here, I could never learn about it. At the same time, I could learn a lot of physiological knowledge and technique, which will be my advantage.

LONG TERM VALUE

9 How the NRC Associateship award affected your career to date

Comments

I am a foreigner, so if NRC had not given me an opportunity, it was really hard to join in this group and keep my career in USA. Especially, I guess it was not able to study in army institutes without the NRC associateship.

LAB SUPPORT

10 Quality of support from the Laboratory--equipment, funding, orientation, safety and health guidelines, etc.

Comments

It was really good. When I joined the group, I could get my own desk and PC immediately. There were a lot of safety guidance and training for animal handling. All equipment was already ready for experiments.

ADVISER/MENTOR SUPPORT

10 Quality of mentoring from the Laboratory NRC Adviser (USMA Mentor, if applicable)

Comments

All my advisers and mentors have deep and wide knowledge and all of them are specialists in TBI research. They always gave me correct and reasonable suggestions.

LPR SUPPORT

10 Quality of administrative support from the Laboratory (e.g., NIST) NRC Program Representative (LPR)

Comments

It was really good. In processing to Army is really complicated, but they supported me well and it went really smoothly.

NRC SUPPORT

8 Quality of administrative support (applications, inquiries, post-review, award-related, travel, etc.) from the NRC

Comments

Dr. Rothman at WRAIR is taking care of associates really well and she always supports us a lot. She always opens her door for us. I really appreciate about her supports. When I had a questions about administrative things, the NRC people answered as soon as possible, especially, Ms. Wilson at visa office helped and supported me a lot.

18) *PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT.*

Many People, who are foreigner like me, do not know about NRC associateship. If they know it, NRC can give a good opportunity to do research in USA for foreign researchers.

Mail & Delivery Address

It is NOT necessary to mail the original.

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Washington, DC 20001

ID# 0830210

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Rev. Jan. 2008

Suggestions for, or problems with, forms should be directed to the forms manager, Suzanne White, swhite@nas.edu.

CC#

n/a

Domestic

12) *SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES* **Include dates, names and locations of seminars.**

n/a

13) *PROFESSIONAL AWARDS RECEIVED DURING TENURE*

n/a

14) *POST-TENURE POSITION / JOB TITLE*

ORISE Contractor

15) *NAME AND ADDRESS OF POST-TENURE POSITION / JOB ORGANIZATION*

AMRICD, 3100 Ricketts Point Road, Aberdeen Proving Ground, MD 21010-5400

16) *POST-TENURE POSITION STATUS / CATEGORY* **Please indicate only one.**

- ☐ Remain at Host Agency as Permanent Employee
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On a scale of 1 – 10 (poor - excellent), please rate the following:

SHORT TERM VALUE

10 Development of knowledge, skills, and research productivity
Comments

LONG TERM VALUE

10 How the NRC Associateship award affected your career to date
Comments

LAB SUPPORT

10 Quality of support from the Laboratory--equipment, funding, orientation, safety and health guidelines, etc.
Comments

ADVISER/MENTOR SUPPORT

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Comments

LPR SUPPORT

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Comments

NRC SUPPORT

5 Quality of administrative support (applications, inquiries, post-review, award-related, travel, etc.) from the NRC
Comments

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http://www7.national-

Suggestions for, or problems with, forms should be directed to the forms manager, Suzanne

500 Fifth Street NW, #568
Washington, DC 20001

academies.org/rap/Coordinators_with_Agencie ml
If link does not connect, unprotect Word do
or do "Ctrl Click"
Rev. Jan. 2008

White, swhite@nas.edu.

ID#

CC#

Taylor SL, Krempel RL, Schmaljohn CS. (2009) Inhibition of TNF-alpha-Induced Activation of NF-kB by Hantavirus Nucleocapsid Proteins. Submitted to the NY Academy of Sciences.

10) *PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NATIONAL ACADEMIES ASSOCIATESHIP RESEARCH*
Provide titles, inventors, and dates of applications.

11) *PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES*
Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.

International

2008 International Congress of Virology (Istanbul, Turkey)

2006 Negative Strand Viruses (Salamanca, Spain)

Domestic

2008 American Society of Virology (Cornell, NY)

2008 Viral Immunity Keystone Symposia (Keystone, CO)

12) *SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES* **Include dates, names and locations of seminars.**

13) *PROFESSIONAL AWARDS RECEIVED DURING TENURE*

14) *POST-TENURE POSITION TITLE*

ORISE Participant

15) *POST-TENURE ORGANIZATION* **Provide name and address of organization.**

Oak Ridge Insitute for Science and Education
4692 Millenium Drive
Suite 101
Belcamp, MD 21017

16) *POST-TENURE POSITION STATUS / CATEGORY* **Please indicate only one.**

- ☐ Remain at Host Agency as Permanent Employee
- ☒ Remain at Host Agency as Contract/Temporary Employee
  Abbreviate Host Laboratory/Center **USAMRIID**
- ☐ Research Position at Another US Government Laboratory
- ☐ Administrative Position at US Government Laboratory
- ☐ Research Position at Foreign Government Laboratory
- ☐ Research/Teaching at US College/University
- ☐ Research/Teaching at Foreign College/University
- ☐ Research/Administration in Industry
- ☐ Research/Administration in Non-Profit Organization
- ☐ Postdoctoral Research
- ☐ Self Employed
- ☐ Other: **specify** _____

17) *APPRAISAL OF RESEARCH ASSOCIATESHIP PROGRAM*
On a scale of 1 – 10 (poor - excellent), please rate the following:

SHORT TERM VALUE

9 Development of knowledge, skills, and research productivity
Comments

LONG TERM VALUE

9 How the National Academies Associateship award affected your career to date
Comments

LAB SUPPORT

8 Quality of support--equipment, funding, orientation, safety and health guidelines, etc.
Comments

ADVISER/MENTOR SUPPORT

9 Quality of mentoring from the Lab NRC Adviser (USMA Mentor, if applicable)

Comments

LPR SUPPORT

7 Quality administrative support from the LPR
Comments

NRC SUPPORT

7 Quality of administrative support from the NRC
Comments

18) *PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT.*

Gideon Wasserberg, Richard Poche, Larisa A Polyakova, V. Michelle Chenault, Gabriela Zollner, Edgar D Rowton, David Miller. To be submitted to J. Med. Entomol.

10) *PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH*
Provide titles, inventors, and dates of applications.

11) *PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES*
Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.

International

ISOPS 6, October 2008, Lima Peru:
1. Wasserberg, G. The Ecology of Cutaneous Leishmaniasis in Israel: Demographic and Spatial aspects of the vector – reservoir host relationship
2. Wasserberg, G; Rowton, E., Miller, D. Feed-Through Control for Larval Sand Flies Using Host-Targeted Insecticide.
3. Rowton, E; Wasserberg, G. What do Sand-flies Want? Unveiling Secrets of Host and Plant Attraction.

Domestic

ASTMH, November 2009, DC
Gideon Wasserberg, Richard Poche, Larisa A Polyakova, V. Michelle Chenault, Gabriela Zollner, Edgar D Rowton, David Miller. Feed-Through Control for Larval Sand Flies Using Host-Targeted Insecticide.

Ecology and Evolution of infectious diseases, Athens , Georgia
Gideon Wasserberg, Erik E. Osnas, Robert E. Rolley, and Michael D. Samuel. Host culling as an adaptive management tool for chronic wasting disease in white-tailed deer: a modeling study.

12) *SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES* **Include dates, names and locations of seminars.**

01/12/2009. Wyoming department of veterinarian sciences: Emergence and resurgence of zoonotic and wildlife diseases.
01/21/2009. Dutch Wildlife health center, University of Utrech, The Netherlands: Landscape epidemiology and mathematical modeling: approaches for the study and control of zoonoses and wildlife diseases.
02/04/2009. Biology Department, University of North Carolina at Greensboro. Landscape epidemiology and mathematical modeling: approaches for the study and control of zoonoses and wildlife diseases.

13) *PROFESSIONAL AWARDS RECEIVED DURING TENURE*

14) *POST-TENURE POSITION / JOB TITLE*

Assistant Professor

15) *NAME AND ADDRESS OF POST-TENURE POSITION / JOB ORGANIZATION*

Department of Biology, University of North Carolina at Greensboro.

16) *POST-TENURE POSITION STATUS / CATEGORY* **Please indicate only one.**

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- ☐ Research/Administration in Non-Profit Organization
- ☐ Postdoctoral Research
- ☐ Self Employed
- ☐ Other: **specify** _____

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On a scale of 1 – 10 (poor - excellent), please rate the following:

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9 Development of knowledge, skills, and research productivity
Comments

LONG TERM VALUE

9 How the NRC Associateship award affected your career to date

Comments
KNowledge and contacts

LAB SUPPORT

9 Quality of support from the Laboratory--equipment, funding, orientation, safety and health guidelines, etc.
Comments

ADVISER/MENTOR SUPPORT

9 Quality of mentoring from the Laboratory NRC Adviser (USMA Mentor, if applicable)
Comments

LPR SUPPORT

9 Quality of administrative support from the **L**aboratory (e.g., NIST) NRC **P**rogram **R**epresentative (LPR)
Comments

NRC SUPPORT

8 Quality of administrative support (applications, inquiries, post-review, award-related, travel, etc.) from the NRC
Comments
Often hard to contact representative on the phone and at times slow on email reply

18) *PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT.*
Improve medical insurance

Mail & Delivery Address

It is NOT necessary to mail the original.
The National Academies
NRC Research Associateship Programs
500 Fifth Street NW, #568
Washington, DC 20001

ID# 0811850

This form SHOULD be E-MAILED directly to the NRC Coordinator.

http://www7.national-academies.org/rap/Coordinators_with_Agencies.html
If link does not connect, unprotect Word doc, or do "Ctrl Click"
Rev. Jan. 2008

Suggestions for, or problems with, forms should be directed to the forms manager, Suzanne White, swhite@nas.edu.

CC#

b) **Books, book chapters, other publications**

None

c) **Manuscripts in preparation, manuscripts submitted**

None

10 *PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM THE NRC ASSOCIATESHIP RESEARCH PROGRAM*

Provide titles, inventors, and dates of applications.

None

11) *PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES*

Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.

International

None

Domestic

None

12) *SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES* **Include dates, names and locations of seminars.**

None

13) *PROFESSIONAL AWARDS RECEIVED DURING TENURE*

None

14) *POST-TENURE POSITION / JOB TITLE*

Post Doctoral Associate, USAMRIID, Virology Department

15) *NAME & ADDRESS OF POST-TENURE POSITION / JOB ORGANIZATION*

USAMRIID
1425 Porter Street, Frederick, MD 21702

16) *POST-TENURE POSITION STATUS / CATEGORY* **Please indicate only one.**

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- [ ] Research/Admin in Non-Profit Organization
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5 Quality of support from the Laboratory--equipment, funding, orientation, safety and health guidelines, etc.
Comments

ADVISER/MENTOR SUPPORT

3 Quality of mentoring from the Laboratory NRC Adviser (USMA Mentor, if applicable)
Comments

He conveys a poor attitude towards the institute and is apathetic about research in general. I understand not loving your job, but because of this he had little motivation to perform new research. He was very closed to new ideas.

LPR SUPPORT

3 Quality of administrative support from the **L**aboratory (e.g., NIST) NRC **P**rogram **R**epresentative (LPR)
Comments

The administrative support from the LPR was fine, but it was clear he does not want to be involved with any issues that arise.

NRC SUPPORT

7 Quality of administrative support (applications, inquiries, post-review, award-related, travel, etc.) from the NRC
Comments

18) *PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT.*

There needs to be more support for fellows who are having problems with their current advisor. I found an advisor that was willing to allow me to continue this work, but was denied further research support by the LPR and NRC.